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The American Heart Journal

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The American Heart Journal

VOL. 9 FEBRUARY, 1934 NO. 3

Original Communications

HEART DISEASE FROM THE POINT OF VIEW OF THE PUBLIC HEALTH—1933*†

ALFRED E. COHN, M.D., AND CLAIRE LINGG, M.A.
NEW YORK, N. Y.

WHETHER the death rate from "heart disease" is increasing is still the subject of active debate. A report was made dealing with several aspects of this problem in 1926.[1] Since then, the number has seemed to be mounting[2] though doubt concerning the correctness of this belief has been expressed by responsible public health officers.[3] The present report was undertaken to continue the study begun in 1926.

Certain preliminary decisions have necessarily been taken. The curves published in 1926 described the course of events in the original ten registration states and the District of Columbia. It seemed wise therefore to continue to confine this study to this area. These states, the registration area of 1900, comprised the states of New England, New York, New Jersey, Indiana, and Michigan. This plan has two advantages: first, the record is the longest available in the United States; and second, this area presents, within not too wide limits, similarity of climate. There is a third advantage; the area is large. Inferences drawn from occurrences here are less likely to be unduly sensitive to modifying local influences. Local influences may indeed issue in consequences of considerable importance. Evidence is, as a matter of fact, becoming available which suggests that the course of rheumatic fever and its lesions may actually differ with latitude and longitude, with humidity, with the quality of sunlight. In short, the natural history of a disease elsewhere need not be identical with that in the registration area of 1900. Conversely, a description of an area as a whole need not be applicable to a subdivision of that area, to New York City for example. The area may be regarded as the

*From the Hospital of the Rockefeller Institute for Medical Research, New York, and the Heart Committee, New York Tuberculosis and Health Association, New York.

†Based on a report made to The American Public Health Association, Washington, D. C., October 24, 1932.

"hinterland" of the cities. What occurs in any section of it may have legitimate geographical interest, but is less significant when the subject of study is the course of a disease. Continuing to confine this study to the same states has another advantage. It suggests the advisability of making parallel studies in other regions differing in climate, light, altitude. Differences may be found not only in the course of rheumatic fever but in the behavior of other cardiac affections as well. Comparison may be expected to deepen insight into the nature of these various processes.

In the summary of the report of 1926 these paragraphs appear:

3. It is borne out by study of the curves which relate infectious and heart diseases, that the two have moved in opposite directions. The curve which represents the former has been falling, while that of the latter has risen. But the relation is not quite simple, for neither curve travels a smooth course. It is, however, possible to notice that at certain points, changes in the direction of both curves have taken place. It is furthermore noticeable that there occurred a delay in the increased rise of the curve from heart disease for a number of years after that of the infectious diseases began to fall. That this period is seventeen years may have a meaning but it is not an obvious one and no insistence is placed upon it. That there should be a delay like this is easily comprehended; if individuals fail to die of infection, they will die in some other manner, and of affections which develop or are incident to life at later ages.

4. That the data which have been accumulated support this view seems clear, for the curves all show that the increased rate of death from the heart diseases involves persons over age forty. Under this age, the rates, as these curves show have actually fallen. Additional confirmation of this view resides in the fact that the rate increases with each decade.

These opinions form the starting point of this further study. The curves* carried formerly to 1923 (Figs. 1 and 2) now include the facts to the year 1930. They show that the direction of the slopes of the curves remains unchanged. The inference that a relation exists between decrease in deaths from infectious diseases, and increase in those from other causes in later decades, especially from the heart diseases, seems still to be justified. Since 100 per cent of the population dies, the outstanding question becomes "When?" To discover this, curves of the death rates at each decade (the specific death rates) were constructed (Fig. 2). In the heart diseases they show that *before* the age of forty the rates had been falling steadily since the year 1900; and that *after* the age of forty, they rose, and did so the higher, the older the age group. Recently, since 1920, in the older decades, they show a tendency to flatten. In the infectious diseases they show that the rates were falling and were doing so in *every* decade. This is a matter of importance to which it will be necessary later to return.

*We are indebted to Miss Whittemore and the other members of the staff of the Research Committee of the New York Heart Committee for their aid in constructing these curves. We are under great obligation to the Bureau of the Census, and to Dr. Murphy for transcribing the figures necessarily used in making the curves. We wish especially to express our indebtedness to him for his courtesy and cooperation.

Under these circumstances the deduction seemed simple and justified that freedom from infectious diseases, known to have taken place on a large scale, has resulted naturally in increase in the number and

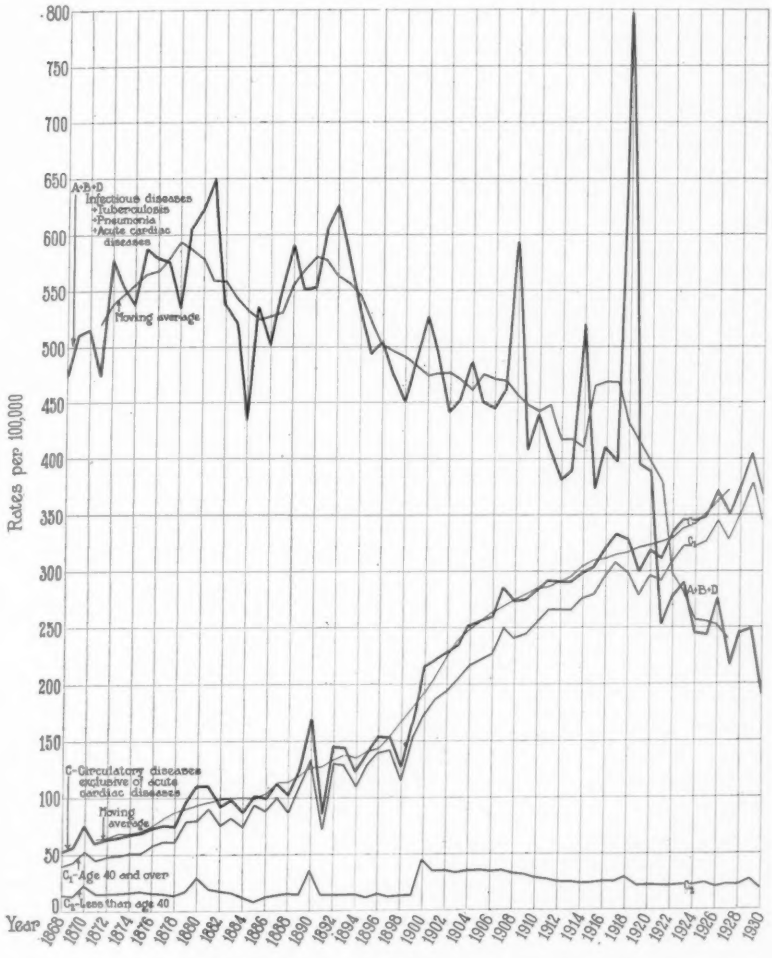


Fig. 1.—These curves exhibit the mortality rates per 100,000 of various diseases in the First Ten Registration States plus the District of Columbia from 1868-1930. Curve A+B+D describes the course of events when infectious diseases, tuberculosis, the pneumonias and acute cardiac diseases are added; Curve C, that in circulatory diseases, exclusive of acute cardiac diseases; Curve C_1 includes of Curve C, only those age forty and over; C_2 includes of Curve C, only those less than age forty.

Diseases grouped as follows:

A—(Infectious diseases)
Typhoid fever
Measles
Scarlet fever
Whooping cough
Diphtheria
Influenza
Mumps
Dysentery
Acute poliomyelitis
Meningococcal meningitis
Malaria
Cholera nostras

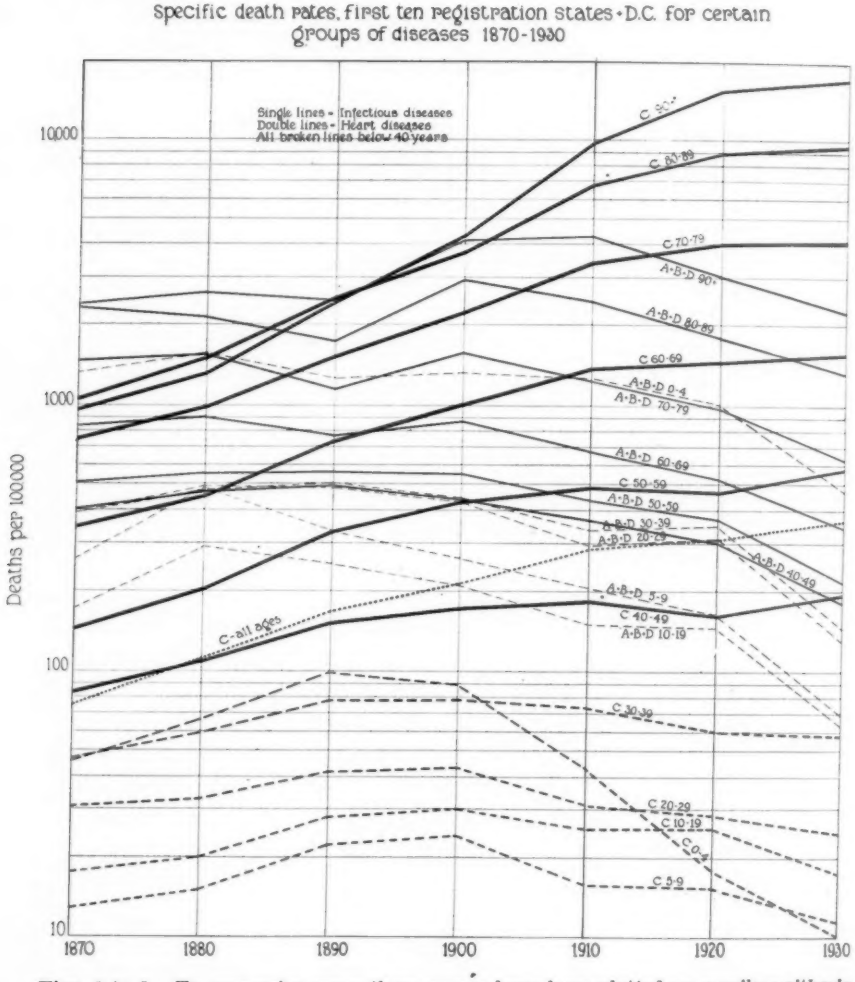
B—Tuberculosis
Pneumonia
Bronchopneumonia

C—(Circulatory diseases exclusive of acute cardiac diseases)
Apoplexy
Angina pectoris
Other diseases of the heart (including endocarditis)
Diseases of the arteries
Other diseases of the circulatory system.

D—(Acute cardiac diseases)
Pericarditis
Acute endocarditis and myocarditis

States included: Connecticut, Indiana, Maine, Massachusetts, Michigan, New Hampshire, New Jersey, New York, Rhode Island, Vermont, and District of Columbia.

in the rate of deaths from other causes in later decades. Further reflection has suggested that in this simple deduction error has found its way. If in the year 1900 for example, the death *rate* from chronic diseases of the heart in a given later decade of life is expressed by a certain figure, why, in the same decade at another date, such as 1930, should a change take place? At the two dates, in any 100,000 persons



Figs. 2 to 8.—To economize space these curves have been plotted on semilogarithmic scales. The data refer in each one to the Registration States of 1900 plus the District of Columbia. These curves give specific death rates. The designations of the curves used are the same as those in Fig. 1.

of this age, approximately the same number of persons should die. The *rate* should remain unchanged, though with increase in population the *number* of deaths would, of course, rise. This statement is made categorically and requires now qualification on two important counts. First: if certain members of each group of 100,000 have sus-

tained injuries *in earlier years,* from scarlet fever or from diphtheria for example, of such a nature as to predispose them to disease of the heart, the number and rate of deaths from heart disease among them might, presumably, be greater than among those who had not experienced these illnesses. This suggestion has actually been made.[4] The correctness of this supposition is, at the present however, not open to analysis; there are no suitable reports of morbidity. Until these, so seriously wanted, are supplied, neither this nor other similar suggestions can be tested. Whether it is important to make this analysis will appear on further consideration.

The second qualification arises from the possibility that the death rate in a decade of age is modified by changes taking place *in that decade itself.* This possibility can be studied. If, for example, of 100 persons aged sixty, 10 persons formerly died of pneumonia but do so no longer, dying now of a heart disease instead, the number who die of a heart disease is increased by the number no longer dying of pneumonia. The saving from infectious diseases has in fact been more than great enough in the sixth and tenth decades themselves to account for the increase in the number of deaths per 100,000 from the heart diseases, but in the seventh, eighth, and ninth, they were not, although the savings in these decades attained considerable dimensions (Table I). Other causes must account for the increase.

To do so, search may be instituted in another direction. The inquiry shifts now to consideration of "fashion" in diagnosis.[3] Changes

TABLE I

CIRCULATORY AND RENAL DISEASES

AGE	(A B C D E)* 1900	1930	INCREASE
40-49	261.8	250.7	−11.1
50-59	598.1	721.3	+123.2
60-69	1389.9	1962.3	+572.4
70-79	3478.9	5048.5	+1569.6
80-89	8895.0	11908.5	+3013.5
90+	21053.7	22090.4	+1036.7

INFECTIOUS DISEASES†

AGE	(1) 1900	(2) 1930	(3) DECREASE	(4) INCREASE IN A B C D E	(4) − (3)
40-49	447.7	183.8	−263.9	−11.1	
50-59	555.2	231.6	−323.6	+123.2	−200.4
60-69	876.7	345.5	−531.2	+572.4	+41.3
70-79	1589.6	625.9	−963.7	+1569.6	+605.9
80-89	2970.0	1315.8	−1654.2	+3013.5	+1359.3
90+	4188.5	2203.4	−1985.1	+1036.7	−948.4

*These letters designate briefly the rubrics shown in Fig. 3.
†The infectious diseases are those designated in Table III.

in the number of deaths entered in a diagnostic rubric are known to take place. The reasons for these changes are numerous. R. L. Levy[5] has shown that in the Presbyterian Hospital in New York City the number of times the diagnosis, thrombosis of coronary arteries, for example, was entered increased sharply after the publication of papers on the subject by J. B. Herrick. Attention was, it seems, focussed sharply on a special form of illness and resulted in greater diagnostic acumen. Reports on this subject to the Bureaux of Vital Statistics in the registration area obviously can influence the form of the curves

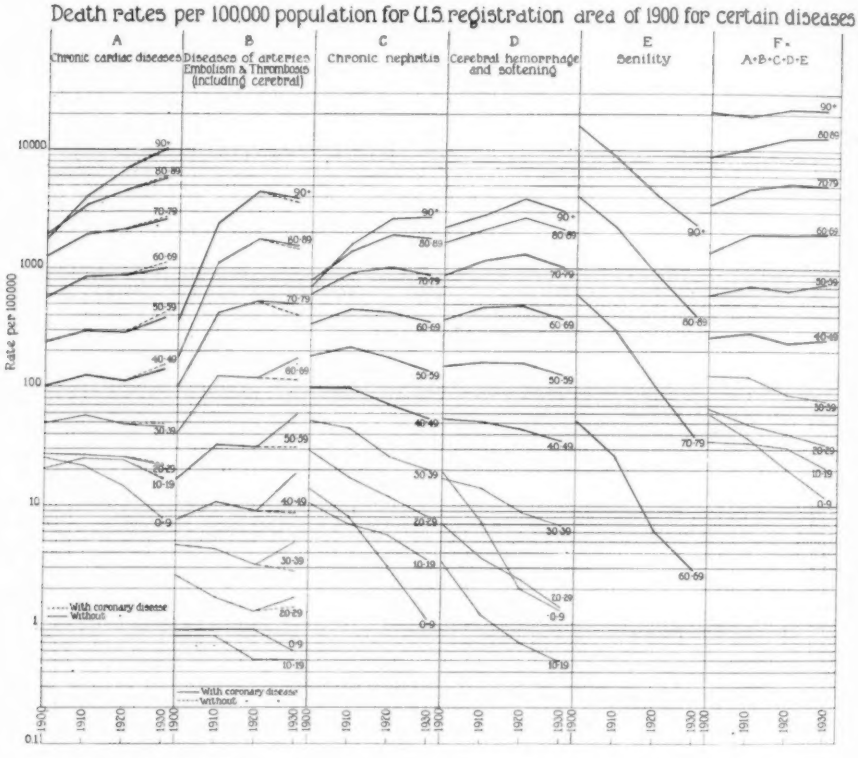


Fig. 3.—A to F. These curves describe the course of the rate of mortality at each decade of life under five separate rubrics for the four years, 1900, 1910, 1920, 1930. A exhibits the situation in chronic cardiac diseases; B, that in diseases of the arteries; C, in chronic nephritis; D, in cerebral hemorrhage and softening of the brain; E, in senility. F gives the rates when these five classes of disease are added. Table II indicates which code numbers are used and the equivalent code numbers in succeeding editions of the International List of Causes of Death.

(Fig. 3, A and B). And again increase in knowledge or further consideration of the problem of classification may account for the violent changes which have taken place under the head of senility (Fig. 3, E).*

Similar changes may have occurred in the categories, "chronic cardiac diseases," "diseases of the arteries," "chronic nephritis," "cere-

*These statements ignore, as they may, difficulties connected with double entries in registration.

bral hemorrhage and softening of the brain," and "senility." Conceivably, for reasons not wholly apparent, cases entered under one may, at another time, be entered under another heading. Scrutiny of all the categories employed in the International List of Causes of Death has singled out those which have just been named as the ones especially liable to change of this sort. Each of them has in fact undergone alteration (Fig. 3, A, B, C, D, E). If, instead of making the effort to understand the behavior of each class separately, this group of chronic ailments is regarded as a whole, as a unit, a better insight into what has been the course of events may be secured. When this is done it becomes obvious that the death rate in each decade of life be-

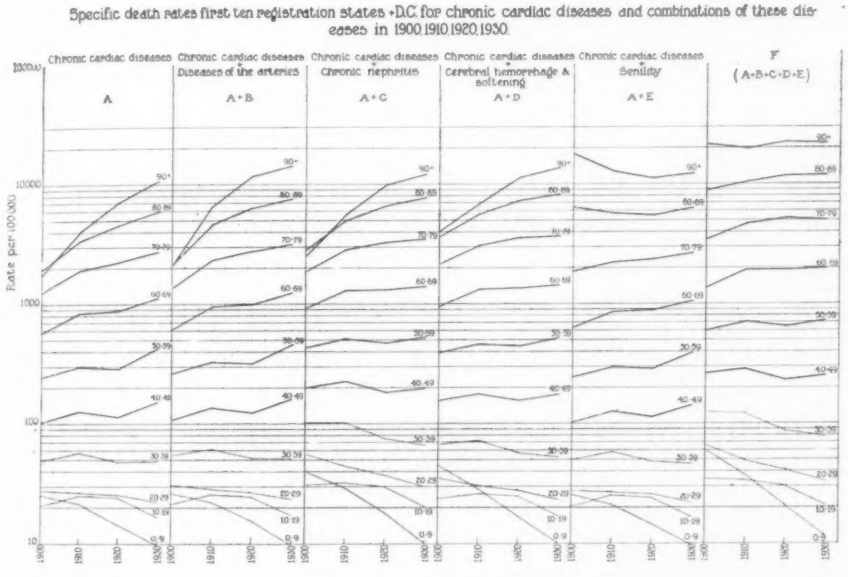


Fig. 4.—These curves describe the course of the death rate at each decade of life in the rubric "chronic cardiac diseases" and combinations of these rates with other selected rates:

A. The rates for chronic cardiac diseases are given separately and are identical with those in Fig. 3, A.
A+B. The rates for chronic cardiac diseases are combined with those of diseases of the arteries (Fig. 3, A+B).
A+C. The rates for chronic cardiac diseases are combined with those of chronic nephritis (Fig. 3, A+C).
A+D. The rates for chronic cardiac diseases are combined with those of cerebral hemorrhage and softening (Fig. 3, A+D).
A+E. The rates for chronic cardiac diseases are combined with those of senility (Fig. 3, A+E).
F. The rates given for these five classes of disease are added. This set of curves is identical with those in Fig. 3, F.

ginning with the fifth has remained much more nearly constant; the curves have become much more nearly flat (Fig. 3, F). This observation may be described in another way; when the effort to arrange the cases under appropriate but arbitrary rubrics is ignored, and a more general scheme of classification is adopted, descriptive nevertheless of the group, the members within which are reasonably closely related,

a sharp increase has obviously not occurred. Even if to the class "chronic cardiac diseases" (Fig. 4, A) that of "senility" (Fig. 3, E) alone is added, the resulting curve (Fig. 4, A+E) presents a form in striking contrast to that of the two component curves. But whether the group is regarded as a whole (Fig. 4, F) or merely from the point of view of a combination of "chronic cardiac diseases" and "senility" (Fig. 4, A+E) or of any other combination of which A is one element, the result (Fig. 4) shows that a rise has taken place in the decades beginning with the fifth (except A+C and F), though taken as a whole (Fig. 4, F) the rise is distinctly smaller than is the case when it occurs in any one, singly.

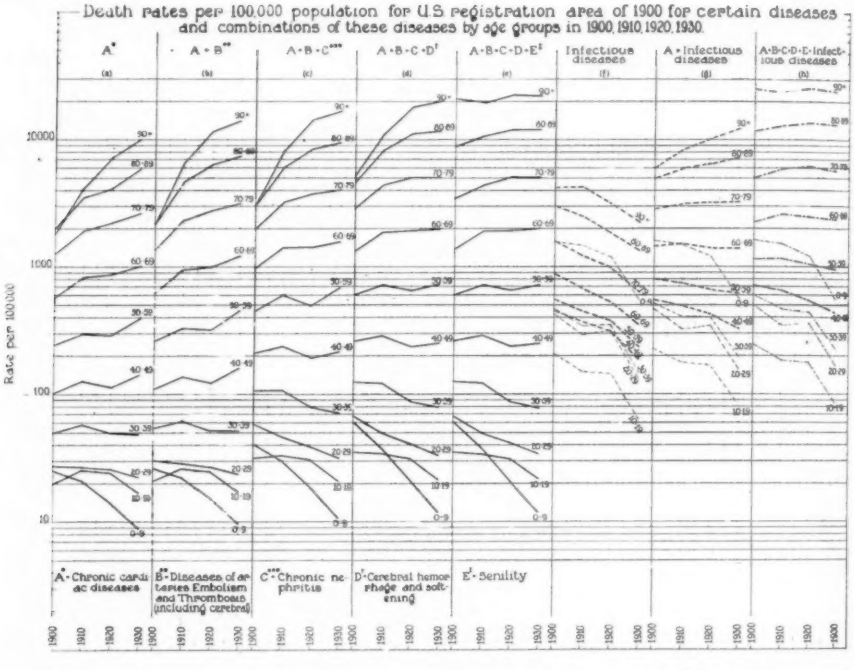

Death rates per 100,000 population for U.S. registration area of 1900 for certain diseases and combinations of these diseases by age groups in 1900, 1910, 1920, 1930.
Rate per 100,000
A* Chronic cardiac diseases
B** Diseases of arteries Embolism and Thrombosis (including cerebral)
C*** Chronic nephritis
D† Cerebral hemorrhage and softening
E‡ Senility
Infectious diseases
A + Infectious diseases
A-B-C-D-E-Infectious diseases

Fig. 5.—These curves describe the course of the death rates at each decade of life in the rubric "chronic cardiac diseases"; of those in the infectious diseases, and of combinations of these with other selected rates.

(a) The rates for chronic cardiac diseases are given separately and are identical with those in Fig. 3, A.

(b) The rates for chronic cardiac diseases are combined with those of diseases of the arteries (Fig. 3, A+B).

(c) The rates for chronic cardiac diseases and diseases of the arteries are combined with those of chronic nephritis (Fig. 3, A+B+C).

(d) The rates for chronic cardiac diseases, diseases of the arteries, and chronic nephritis are combined with those of cerebral hemorrhage and softening (Fig. 3, A+B+C+D).

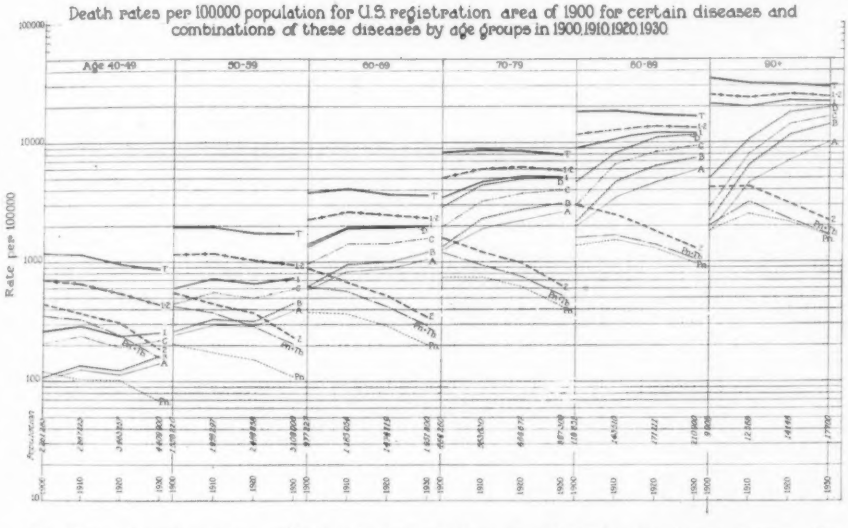
(e) The rates for chronic cardiac diseases, diseases of the arteries, chronic nephritis, cerebral hemorrhage, and softening are combined with those of senility (Fig. 3, A+B+C+D+E). This set of curves is identical with those in Fig. 3, F.

(f) These curves describe the course of the death rates at each decade of life in the infectious diseases. Table III indicates which items are used and the equivalent code numbers in succeeding editions of the International List of Causes of Death.

(g) The rates of chronic cardiac diseases (a) and infectious diseases (f) are combined.

(h) The rates in (e) and infectious diseases (f) are combined.

If the course of events in the infectious diseases is now considered again, the meaning of the fall in the death rate compared with that of the circulatory group becomes apparent (Fig. 5). It is in these two great groups, the infectious and circulatory diseases (inclusive of chronic nephritis) in which by far the majority of all deaths is included. The two together should approximate the total death rate. The addition does in fact correspond with this assumption; the interval between the sum (Fig. 6, Curve 1·2) and the total rate (Fig. 6, Curve T) is relatively small and has become steadily smaller with time. But the result of the addition presents a new problem. In the fifth, sixth, and tenth decades, as the curves (Figs. 6 and 7 in comparison with Fig. 3, Curve F and Table I) show, the decreases in infectious diseases are greater than the increases in the circulatory group.



In Figs. 6 and 7 the method of presentation is changed. In these figures the data are arranged not according to diseases, but according to age. In each column are given data concerning the circulatory group and the infectious group.

Fig. 6.—Curve A describes the course of the death rates in chronic cardiac diseases.
Curve B adds to Curve A the death rates in diseases of the arteries.
Curve C adds to Curve B the death rates in chronic nephritis.
Curve 1 in the fifth and sixth decades adds to Curve C the death rates in cerebral hemorrhage and softening and represents therefore the death rates of this entire circulatory group.
Curve D beginning in the seventh decade adds to Curve C the death rates in cerebral hemorrhage and softening.
Curve 1 beginning with the seventh decade, adds to Curve D the death rates in senility and represents therefore the death rates of this entire circulatory group.
Curve Pn gives the death rates from the pneumonias.
Curve Pn+Tb adds to Curve Pn the death rates from tuberculosis.
Curve 2 adds to Curve Pn+Tb the death rates of *all* the other infectious diseases. For the code numbers used of the infectious diseases, see Table III.
Curve 1·2 is the sum of Curve 1 and Curve 2.
Curve T adds to Curve 1·2 the death rates of *all* the other causes of death and describes therefore the total death rate.

The slope of the curves is downward (difference between 1900 and 1930). The meaning of this seems to be that the effect of saving from infectious diseases continues to result in a positive balance (decrease

TABLE II

CODE NUMBERS OF CHRONIC CARDIAC DISEASES, DISEASES OF THE BLOOD VESSELS, AND OF THE KIDNEYS IN SUCCEEDING EDITIONS OF THE MANUAL OF THE INTERNATIONAL LIST OF CAUSES OF DEATH

YEAR	CHRONIC CARDIAC DISEASES	CHRONIC NEPHRITIS	DISEASES OF THE ARTERIES EMBOLISM AND THROMBOSIS (INCLUDING CEREBRAL)	CEREBRAL HEMORRHAGE AND CEREBRAL SOFTENING	SENILITY
1900 (List published 1902)	79. Organic diseases of heart 80. Angina pectoris	120. Bright's disease	81. Diseases of the arteries, atheroma, aneurysm, etc. 82. Embolism and thrombosis	64. Congestion and hemorrhage of brain 65. Softening of the brain	154. Senile debility
1910 (1909 revision used)	79. Organic diseases of heart 80. Angina pectoris	120. Bright's disease	81. Diseases of the arteries, atheroma, aneurysm, etc. 82. Embolism and thrombosis	64. Congestion and hemorrhage of brain 65. Softening of the brain	154. Senility
1920 (1909 revision used)	79. Organic diseases of heart 80. Angina pectoris	120. Bright's disease	81. Diseases of the arteries, atheroma, aneurysm, etc. 82. Embolism and thrombosis	64. Congestion and hemorrhage of brain 65. Softening of the brain	154. Senility
1920 (revision used for Fig. 8)	89. Angina pectoris 90. Other diseases of heart	129. Chronic nephritis (including unspecified, 10 yr. and over)	74b. Cerebral embolism and thrombosis 91. Diseases of arteries a. Aneurysm b. Arteriosclerosis c. Other diseases of arteries 92. Embolism and thrombosis (not cerebral)	74a. Cerebral hemorrhage 83. Softening of the brain	164. Senility

TABLE II—CONT'D

YEAR	CHRONIC CARDIAC DISEASES	CHRONIC NEPHRITIS	DISEASES OF THE ARTERIES EMBOLISM AND THROMBOSIS (INCLUDING CEREBRAL)	CEREBRAL HEMORRHAGE AND CEREBRAL SOFTENING	SENILITY
1930 (1929 revision used)	92. Chronic endocarditis, valvular diseases a. Endo. specified as chronic, and other valv. diseases b. Endo. unspecified (45 yr. and over) 93. Diseases of the myocardium c. Chronic myocarditis and myocardial degeneration d. Unspecified 94. Diseases of coronary arteries and angina pectoris a. Angina pectoris (b. Diseases of coronary arteries) 95. Other diseases of the heart a. Functional diseases of the heart b. Other and unspecified	131. Chronic nephritis 132. Nephritis, unspecified (10 yr. and over)	82b. Cerebral embolism and thrombosis (94b. Diseases of coronary arteries) 96. Aneurysm (except of heart) 97. Arteriosclerosis (diseases of coronary arteries excepted) 99. Other diseases of the arteries	82a. Cerebral hemorrhage 82c. Softening of the brain	162. Senility

TABLE III

CODE NUMBERS OF INFECTIOUS DISEASES IN SUCCEEDING EDITIONS OF THE MANUAL OF THE INTERNATIONAL LIST OF CAUSES OF DEATH

YEAR	TUBERCULOSIS	PNEUMONIA	OTHER INFECTIOUS DISEASES											
			TYPHOID FEVER	MEASLES	SCARLET FEVER	WHOOPING COUGH	DIPHTHERIA	INFLUENZA	MUMPS	DYSENTERY	ACUTE POLIOMYELITIS	MENINGOCOCCAL MENINGITIS	MALARIA	CHOLERA NOSTRAS
1900 (List publ. 1902)	(26 to 35) incl.	92, 93	1	6	7	8	9	10	Not listed as separate title	14	63 (''Other diseases of spinal cord'') Ac. polio. *not* listed as spec. title	61	4	13
1910 (Revision of 1909 used)	(28 to 35) incl.	91, 92	1	6	7	8	9	10	Not listed as separate title	14	63 (''Other diseases of spinal cord'') Ac. polio. *is* listed as sep. title	61	4	13
1920 (Revision of 1909 used)	(28 to 35) incl.	91, 92	1	6	7	8	9	10	Not listed as separate title	14	63 (''Other diseases of spinal cord'') Ac. polio. *is* listed as sep. title	61	4	13
1930 (Revision of 1929 used)	(23 to 32) incl.	107, 108, 109	1, 2	7	8	9	10	11	Listed under 44 (c) one of several titles, ∴ not included	13	16	18	38	12

in the Curve 1·2, which is reflected in the total rate) until the seventh decade.* Not until the influence of this movement in the infectious diseases comes to an end, can stability in the slopes of all the curves be expected. Completion of the process will, it seems, result in ever higher populations in the decades beyond those in which the saving occurs. Barring the influence of other affections, such as cancer, rises in the circulatory group must consequently occur until these also in turn become stable. This is the result which seems, as a matter of fact, to be taking place. Beginning with the sixth decade, an increase in the circulatory group is apparent until 1910 or 1920; then greater stability begins to occur (Fig. 6).

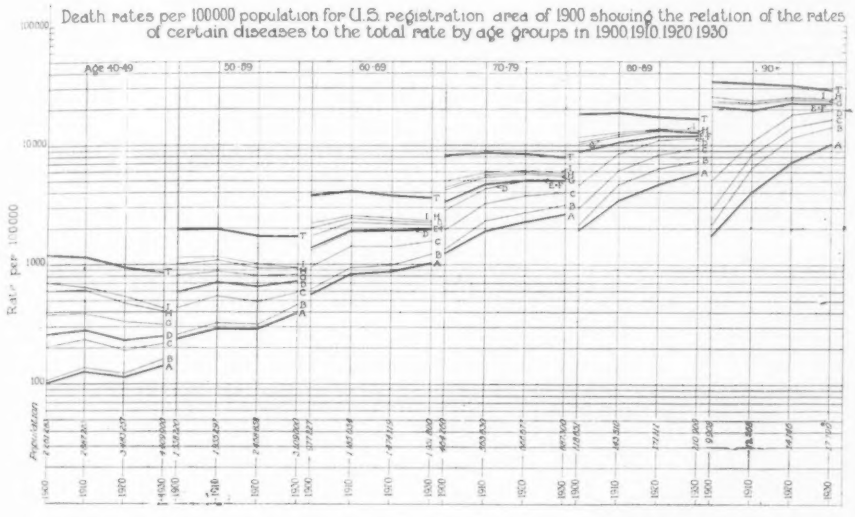

Death rates per 100000 population for U.S. registration area of 1900 showing the relation of the rates of certain diseases to the total rate by age groups in 1900 1910 1920 1930
Age 40-49
50-59
60-69
70-79
80-89
90+
Rate per 100000
Population

Fig. 7.—This is similar to Fig. 6 in that curves A, B, C, D are identical. In the fifth and sixth decades, D (senility) is omitted. The rates of the infectious diseases are given not independently but as additions to the preceding:
In the fifth and sixth decades D and, beginning with the seventh decade, E (= Fig. 3, F) represent the death rates of the entire circulatory group.
Curve G adds to Curve D (fifth and sixth decades) or E (= Fig. 3, F) beginning with the seventh decade, the rates in pneumonias.
Curve H adds to Curve G the rates in tuberculosis.
Curve I adds to Curve H the rates in the other infectious diseases.
Curve T adds to Curve I the rates in *all* the other causes of death and describes therefore the total death rate. It is identical with Curve T in Fig. 6.

As a result of these reflections certain inferences can, it appears, be drawn:

A. 1.—In the later decades the death rate has increased distinctly in A (chronic cardiac diseases) and B (diseases of the arteries); less in the three highest decades in C (chronic nephritis) and D (cerebral hemorrhage and softening of the brain); and has fallen sharply in E (senility) (Fig. 3).

*It seems unnecessary to attribute to savings (from scarlet fever, for example) *in early life*, an influence which does not become operative, even in a small way, until the seventh decade.

2.—If the circulatory and renal group is studied as a whole (Fig 3, F) with the view to ignoring fashions in diagnoses, reflecting in part as these do increase in knowledge, especially of an anatomical nature, increases in the death rate are observable beginning with the sixth decade but the increases are slight in comparison with what have been regarded as the facts, based on a consideration of "chronic cardiac diseases" alone, and have tended to mount relatively little since 1910.

B. The rates in infectious diseases have fallen in every decade (Fig. 5).

C. 1.—If the rates in the two groups (circulatory and infectious) are added (Figs. 5, 6, and 7), the death rate tends to attain equilibrium.

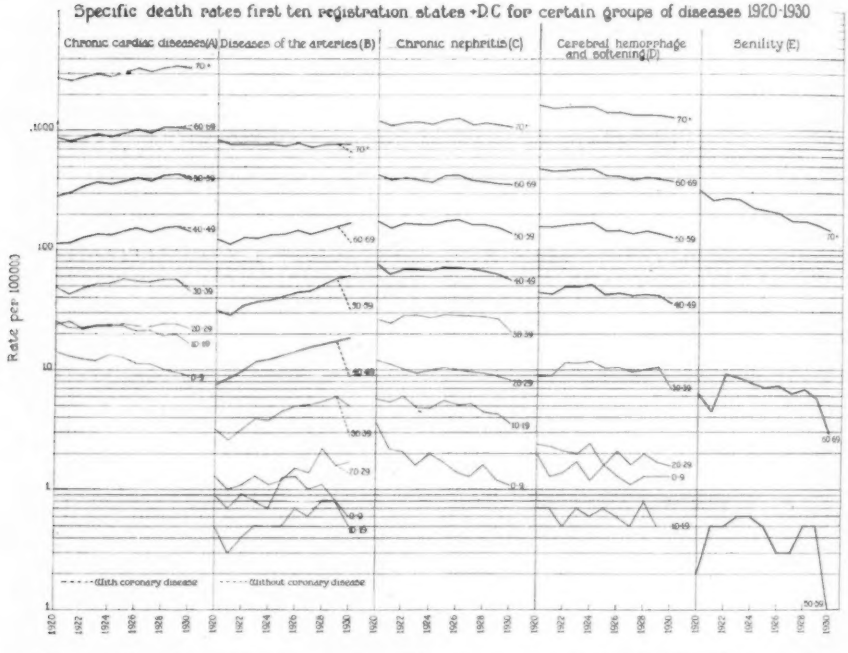

Specific death rates first ten registration states +D.C for certain groups of diseases 1920-1930
Chronic cardiac diseases(A)
Diseases of the arteries(B)
Chronic nephritis(C)
Cerebral hemorrhage and softening(D)
Senility(E)
Rate per 100000
With coronary disease
Without coronary disease

Fig. 8.—The plan of the curves describing the course of the death rates resembles Figs. 3, 4 and 5. It deals with the same rubrics A, B, C, D, E, but analyzes the data in a single decade only, from 1920 to 1930. The influence of the rates of the diseases of the coronary arteries is exhibited.

2.—In point of fact the decrease in infectious diseases is of such importance in the sixth decade that the combined rate has continued to fall, but is in the seventh decade almost unchanged (Fig. 6). Only in the eighth and ninth decades has the rate of circulatory diseases risen enough to elevate the combined rate.

3.—The fall in the total death rate observable in all decades is due to the fall in the rates in the infectious diseases. It is of great importance to point out that the saving from infectious dis-

eases is due *not* to saving in the early decades (though this is possible) for no evidence that this is so is available, but due to saving in these later decades themselves.*

D. A consequence of this analysis is that belief in the theory that "stress and strain" of life accounts for increase in the death rate of the cardiac diseases is unnecessary. The current state of affairs is due not to malign but to beneficent influences.

E. A detailed study of the rates fom 1920 to 1930 (Fig. 8) shows that in A (chronic cardiac diseases) the rate rose beginning with the fifth decade. Excluding diseases of the coronary arteries the rate in B (diseases of the arteries) scarcely changed except in the third and fifth decades. In C (chronic nephritis), D (cerebral hemorrhage and softening of the brain), and E (senility) the rates fell.

CONCLUSIONS

1. The death rate from circulatory diseases has risen. It has not been great, though "great" is a relative term, and recently the increase has become ever slighter.

2. Misinterpretation of the course of events has resulted largely from changes in the entries in those diagnostic rubrics which have been predominantly employed.

3. The rise in the rate in the circulatory diseases, relatively small though it is, depends largely on the fall in the rate in infectious diseases—not that, as has often been supposed, in early life but the fall in those very decades in which a rise in the circulatory group has taken place.

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*That the slope in the curves T continues to fall in every decade suggests either that the movements in the various causes of mortality have not come to an end or that the vital statistics themselves are incompletely descriptive of the facts.

UNUSUAL SINUS TACHYCARDIA WITH OBSERVATIONS ON VAGAL ACTIVITY

Direct Electrical Stimulation of the Vagus Nerves in Man*

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THE case herein reported presents a number of unusual and interesting features. There was a remarkably rapid sinus tachycardia —200 per minute and more. There was advanced cardiac failure which was apparently due to the rapid heart rate alone. A mistaken original diagnosis led to the procedure of surgical exposure and direct electrical stimulation of the vagus nerves whereby there was demonstrated a failure of vagus control of the heart. We know of no reported case comparable in any of these respects.

CASE REPORT

The patient was a male clerk, forty years of age, weighing 55 kilograms, who was admitted to the hospital April 4, 1931. He had enjoyed good health until three weeks prior to admission when he first noticed palpitation, dyspnea, and weakness. The symptoms began suddenly and became increasingly severe so that in five days he discontinued his work and two days later went to bed.

Physical examination revealed the findings of severe congestive heart failure. There was orthopnea, cyanosis, distention of the neck veins, a large right hydrothorax and a large tender liver. There was no demonstrable peripheral edema. The heart was apparently enlarged and displaced to the left. The heart rate was about 200 per minute; the rhythm was regular; the sounds were loud and ringing; no murmurs were heard. The blood pressure was 110/95.

The Kahn reaction was negative. Repeated urinalyses were negative. The hemoglobin was 95 per cent (Sahli) and red blood cells were 5,400,000 per cu. mm., with slight variations in subsequent determinations. The white blood cells ranged from 8,200 to 10,700 per cu. mm., except for a leucocytosis of 17,400 on the eighteenth day in the hospital which followed an attack of severe, cramp-like abdominal pain of unknown origin and which promptly subsided. The basal metabolic rate, determined later when it became practicable, was minus 1 per cent.

Teleroentgenographic measurements of the heart size on admission, during convalescence and after two years of observation are tabulated in Table I. The calculations are based on the prediction tables of P. C. Hodges and Eyster[1] and of F. J. Hodges and Eyster.[2]

An electrocardiogram showed a tachycardia with a rate of 203 per minute. Ventricular complexes were of normal outline. The auricular complexes were partially fused with the T-waves. The cardiac rate and rhythm were not influenced by pressure upon the carotids or the eyes, and a diagnosis of paroxysmal tachycardia of supraventricular origin was made.

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An energetic attempt was made to interrupt the supposed paroxysmal tachycardia. Although the patient had received an unknown amount of digitalis before admission, he was given over a period of five days 2.8 grams of this drug—70 per cent more than the calculated digitalizing dose.

TABLE I

TELEROENTGENOGRAPHIC DETERMINATIONS OF HEART SIZE

DATE	HEART AREA SQ. CM.			TRANSVERSE DIAMETER MM.		
	PREDICTED	MEASURED	VARIATION	PREDICTED	MEASURED	VARIATION
4/ 4/31	111.2	179	+60.9	125.4	175.	+39.6
6/ 7/31		135	+21.4		148.	+18.0
4/19/33		132	+18.9		143.	+14.4

He was also given each day either quinine hydrochloride intravenously (two doses of 0.5 gram and 0.65 gram) or quinidine sulphate orally in increasingly

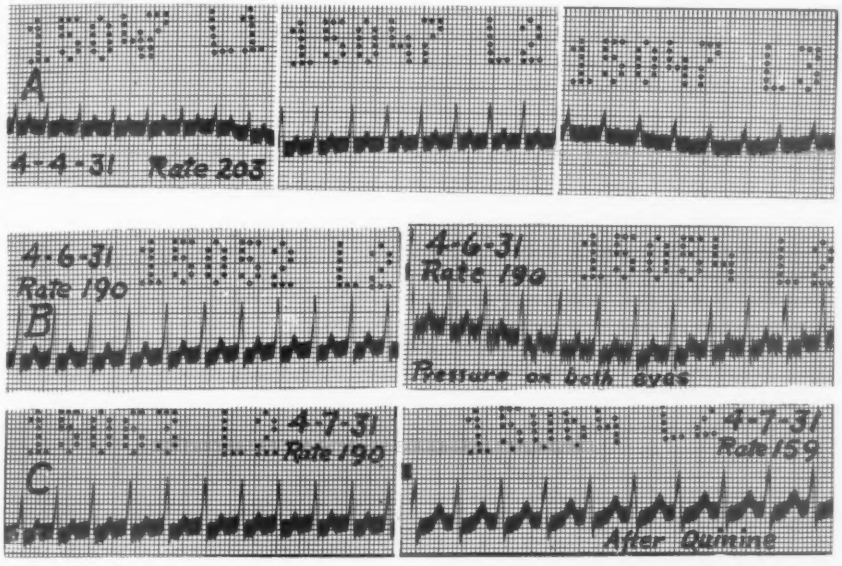

Fig. 1. *A.*—April 4, 1931. The three standard leads taken on admission. Extreme sinus tachycardia. These curves were originally interpreted as indicating paroxysmal auricular tachycardia. *B.* April 6, 1931. Lead II before and during pressure upon both eyes. No change in rate. *C.* April 7, 1931. Lead II before and immediately following the intravenous injection of 0.65 gram of quinine hydrochloride. The rate fell from 190 to 159 per minute.

large and frequent doses. The maximum dosage of quinidine sulphate was 3.2 grams in four doses at hourly intervals. Following the intravenous doses of quinine hydrochloride there was a slowing of the heart rate from 190 to 157 and 159 per minute, respectively, which lasted less than an hour. (Fig. 1.) Following the large oral doses of quinidine sulphate there was a comparable reduction in heart rate to as low as 144 per minute which lasted for several hours. At various times nausea, vomiting, vertigo, and mental confusion occurred. On April 9, 0.4 mg. of apomorphine was given without effect other than vomiting.

None of these measures having produced a lasting effect on the heart rate, the condition of the patient became progressively worse. The right chest was aspirated three times (on April 4, 5, and 8) and a total of 2500 c.c. of fluid was removed. Dyspnea was severe. An abundant, blood-stained, foamy sputum developed. The

patient appeared to be moribund. In what seemed to be a last desperate hope of restoring normal rhythm, direct stimulation of the vagus nerves was determined upon.

On April 10, 1931, under novocaine anesthesia locally, the left vagus nerve was exposed and isolated 2 cm. below the bifurcation of the common carotid artery. It was insulated from the patient's body by rubber dam tissue and then stimu-

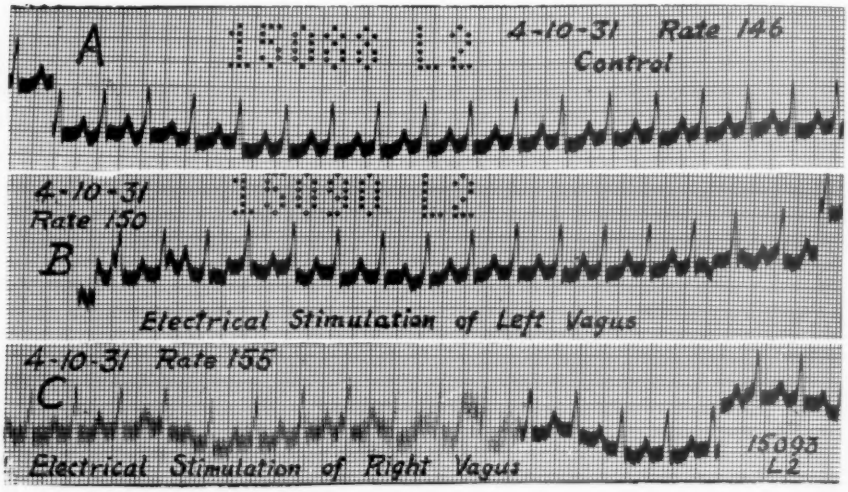

Fig. 2.—April 10, 1931. Lead II. *A*. Control. Rate 146. *B*. During and immediately following electrical stimulation of the left vagus nerve. Rate 150. *C*. During and immediately following electrical stimulation of the right vagus nerve. Rate 155. The oscillations caused by the faradic stimulation are plainly visible. In *B* the oscillations were of such large amplitude and the movements of the string so rapid that they cannot be seen in the record. The beginning of the curve marks the cessation of stimulation.

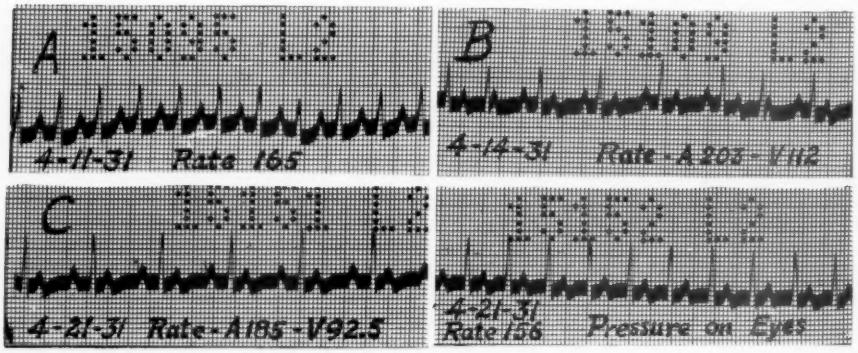

Fig. 3.—Lead II. *A*, April 11, 1931. Curve taken on the day following electrical stimulation of the vagi. *B*. April 14, 1931. Partial A-V heart-block. *C*. April 21, 1931. Pressure upon the eyes slowed the auricles but abolished the A-V block.

lated electrically by faradic current. The current was obtained from an ordinary dry cell and induction coil. At first the nerve was stimulated with a very weak current insufficient to cause contraction of the ribbon muscles of the neck when applied directly to them. When this was without demonstrable effect upon the heart rate, the strength of the current was gradually increased. Finally, the nerve was stimulated directly with a current of sufficient strength to cause strong, sustained

contraction of the neck muscles when applied to them. There was, however, no effect upon the heart recognizable by examining the patient or demonstrated in the electrocardiogram which was taken during the entire procedure (Fig. 2). The weaker stimulation caused pain in the neck and throat and spasmodic coughing; the stronger current caused spasmodic arrest of respiration. There were no other demonstrable changes in the patient. The right vagus nerve was then similarly exposed, isolated, and stimulated, with exactly the same results, positive and negative, as had been obtained with the left (Fig. 2). At the completion of the operation the patient's condition appeared in no way worse than at the beginning.

Following the operation the administration of digitalis in amounts approaching the limit of tolerance was continued. The usual daily dose was 0.4 gram and the average daily dose for five months was 0.38 gram. For two weeks 0.4 gram of quinidine sulphate was given by mouth every eight hours.

No effect was apparent at first except that the heart became somewhat slower (Fig. 3, A). The condition of the patient remained very precarious. On the fourth day after the operation (April 14) partial A-V block appeared and soon became a nearly constant 2:1 block (Fig. 3, B). With a slower ventricular rate the patient began to improve and by the end of another week the signs of cardiac failure had

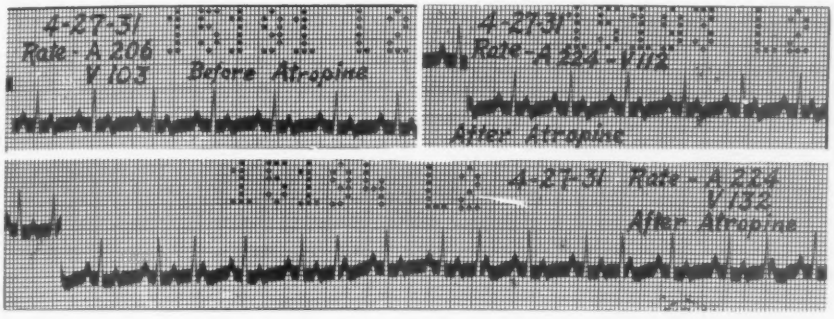

Fig. 4.—Lead II. April 27, 1931. Atropine increased the auricular rate and reduced the A-V block.

cleared. The 2:1 block remained nearly constant for three weeks, during the latter part of which there was a gradual slowing of the auricles. For another week there was a further slowing of the auricular rate with only partial A-V block. Then on May 11, one month after the operation, there was 1:1 response with a rate of 121 per minute. Further reductions in the heart rate and the development of a marked sinus arrhythmia are shown in the electrocardiograms in Fig. 5.

Other interesting electrocardiographic observations on the vagus activity were made during this period of recovery. On April 21, following strong pressure on both eyes the auricular rate slowed from 185 to 156 per minute, the A-V block was abolished, and the ventricular rate increased from 92.5 to 156 per minute (Fig. 3, C). On April 27, atropine sulphate (two doses of 0.5 mg. each, subcutaneously, one half hour apart) increased the auricular rate from 206 to 224 per minute and also reduced the degree of A-V block so that the ventricular rate increased from 103 to 132 per minute (Fig. 4).

The patient has been under observation now for over two years. Rather large doses of digitalis were required at first, to keep the heart rate below 100 per minute (0.4 gram daily for three months after his discharge from the hospital on June, then 0.2 gram daily for five months). Digitalis has been discontinued twice for periods of five and four months, respectively, during which times the pulse rate remained approximately normal. Each time a recurrence of tachycardia which

was markedly exaggerated by mild exercise (up to 200 per minute) has been controlled by 0.15 gram of digitalis daily. Repeated examinations have failed to reveal any evidence of heart disease except the slight residual enlargement noted in Table I.

COMMENT

Because of the gradual slowing of the auricular rate during the second month of observation and the constancy in the form of the P-wave throughout, we believe that we were dealing with sinus tachycardia from the first and that the patient did not have paroxysmal auricular tachycardia. The rate of over 200 is unusual and is ascribed to transient and complete vagal paralysis. The severe congestive heart

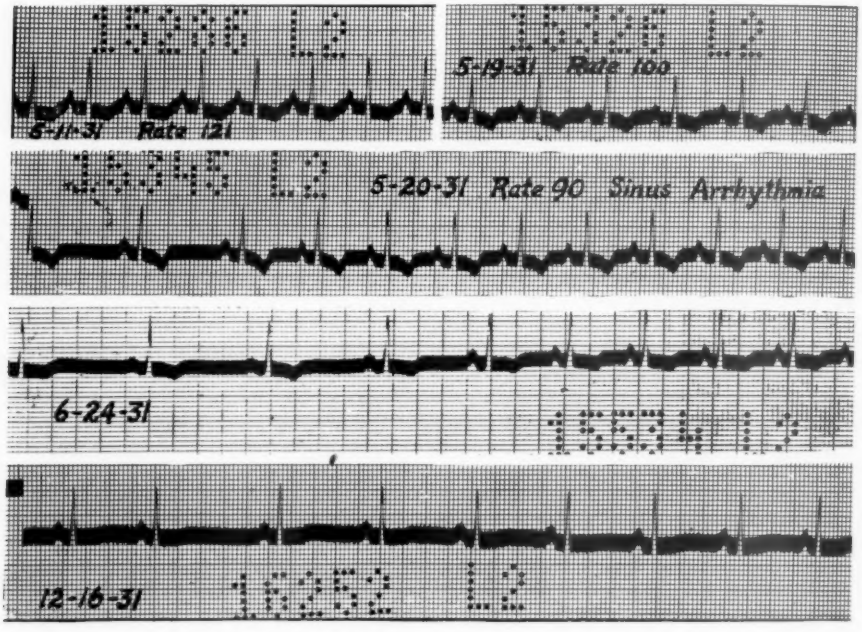

Fig. 5.—Lead II. Curves taken between May 11 and December 16, 1931. The auricles slowed gradually and the block disappeared. The sinus arrhythmia is evidence of more than ordinary vagus action upon the heart. Attention is directed to the uniformity in the contour of *P*. in all figures, indicating that the tachycardia was in reality an extreme sinus tachycardia.

failure which was observed seems to have been due to the rapid heart rate. It was relieved when a slower ventricular rate due to 2:1 block was established. There was no evidence at the time of admission, or in subsequent observations, of any other cause of heart failure, and the patient after more than two years has no symptoms while taking 0.15 gram of powdered digitalis leaves daily.

Failure of vagus action upon the heart was demonstrated, not only by the absence of the usual vagus reflexes, but also by the lack of effect upon the heart of strong faradic stimulation of the exposed vagus nerves. Subsequent observations demonstrated the gradual return of vagus activity.

The observations of April 21, 1931 (Fig. 3), when ocular pressure slowed the auricular rate and at the same time abolished the 2:1 block and increased the ventricular rate, are of interest. There was then a vagus influence on heart rate but no evident influence on A-V conduction. If there was any vagus inhibition of conduction, it was so slight that the slower beating auricles could break through the 2:1 block in spite of it. It would seem that the block had been maintained largely by the direct action of digitalis and quinidine upon the junctional tissues.

On April 27, 1931 (Fig. 4), a return of vagus influence on conduction was demonstrated. On this date the administration of atropine, not only increased the auricular rate, but also reduced the degree of block.

The curves taken between May 11, 1931, and December 16, 1931 (Fig. 5), show a gradual slowing of the auricular rate which is presumed to be due to returning vagus activity. The sinus arrhythmia of May 20, 1931 (Fig. 5), is an indication of quite pronounced vagus tone. The shifting pacemaker observed on June 24, 1931 (Fig. 5), may also be attributed to vagus activity.

SUMMARY

An extreme tachycardia, thought at first to be paroxysmal auricular tachycardia, persisted for four weeks and led to advanced congestive cardiac failure in an otherwise healthy man forty years of age. After the usual methods of interrupting an attack of paroxysmal tachycardia had failed, an attempt was made to terminate the rapid heart action by exposing the vagus nerves in the neck and stimulating them electrically. There was, however, no demonstrable effect upon the heart. Subsequently, partial heart-block, due to digitalis, resulted in slowing of the ventricles and was followed by improvement. Eventually, the auricles gradually slowed, the heart-block disappeared, the cardiac response to vagal activity returned, and the patient recovered. This course of events strongly suggests that the tachycardia was in reality an extreme sinus tachycardia due to failure of vagus inhibition.

The authors gratefully acknowledge the assistance of Dr. F. N. Wilson and Dr. A. G. Macleod in the electrocardiographic studies.

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CONGENITAL COMPLETE HEART-BLOCK*

An Account of Eight Cases

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CONGENITAL complete heart-block is such an uncommon condition that an account of the following 8 cases and of one specimen from the Guy's Hospital Museum is of interest. In a recent review by Yater[29] only 30 of the published cases were accepted as congenital heart-block. He rejected 31 others for lack of sufficient evidence, either owing to the absence of graphic records or because there was a history of some infection which might possibly have been the cause of the block. Probably many of these were genuine cases, but even accepting them all, the number reported has not been very great.

We believe the condition to be more common than would appear from these figures, for we have seen 8 cases in the last six years. It is not difficult for some of them to be missed because the symptoms are generally slight, and the heart rate is faster than in other types of complete block, and the signs of morbus caeruleus are generally absent. If a slow pulse is found in a young man who is an athlete, it is generally sinus bradycardia. But if a slow pulse is found in a child, the possibility of complete heart-block must be remembered, and if it is present and persists, it is likely to be congenital, for infection plays a less important rôle in its production than is sometimes supposed.

Diphtheria is one of the commonest causes of temporary heart-block, which, as a rule, does not last more than a short time: when diphtheria produces a sufficiently severe myocarditis with heart-block, the symptoms are so serious that they are not likely to be missed in determining the cause of heart-block some years later. In a series of 100 cases all followed for more than five years by Jones and White[13] no example of heart-block was found to persist, and in another series of 100 Alstead[3] mentions only one, described fully elsewhere by himself and Chamberlain,[9] where permanent heart-block resulted. Wilkinson[26] has not seen persistent heart-block in the diphtheritic cases he has studied at Birmingham, and Place's experience is the same.[21]

Alstead comments on the curious fact that though temporary complete heart-block is not uncommon in diphtheria, any prolongation of the P-R interval above 0.2 sec. is rarely found without actual A-V dissociation.

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On the other hand, in rheumatic carditis prolongation of the P-R interval is common, but A-V dissociation is rare. We have seen only two examples of complete heart-block due to rheumatism; one has been fully reported[8] and both have made a complete recovery, the P-R interval returning to normal. But we have observed a girl with mitral stenosis, whose P-R interval has been regularly 0.3 sec. for three years and no dropped beat has been noted clinically or in frequent electrocardiograms, though she has been in the hospital twice for considerable periods and has been treated successfully with digitalis (up to dig. fol. gr. 3 daily) for a year.

Rheumatic fever and diphtheria only occasionally cause persistent complete heart-block, and other infectious diseases still more rarely. During the same period (1926-1932) we have seen few other examples of complete heart-block in patients under twenty-five: one may have been syphilitic, for, though her Wassermann reaction was negative, her father had died of general paralysis; the heart-block had not been noticed two years before when she had scarlet fever; so it is possible that the block was caused by this infection. We have no other case in which complete heart-block appeared to follow scarlet fever, and this is also the experience of Place.[21]

The congenital malformation most often found with heart-block is a patent interventricular septum, as shown by a systolic murmur loudest to the left of the sternum. Stokes-Adams attacks are not common, but their occurrence in infancy should be regarded as good evidence of heart-block being congenital if the graphic records are obtained only years later.

The main criteria that heart-block is congenital are:

1. A slow pulse rate at an early age.
2. Signs of congenital morbus cordis, which add considerable weight.
3. The absence of any history of infection; this is additional evidence, but is less important if the first two conditions are present.
4. Syncopal attacks in early childhood or infancy; these would be very suggestive, though such a history is not common.

We have used these criteria in diagnosing our 8 cases as of congenital origin. Four were male and 4 were female. In all of these 8 patients complete heart-block was confirmed by the electrocardiogram. So far as we know the block always remained complete; at times short records were obtained which might have been 2:1 block, but it seemed more likely that these were due to the auricle being about twice as fast as the ventricle, for we never obtained any evidence of a sudden change (Fig. 9, Lead II and Fig. 15, Lead III). At times in some cases the heart rate was faster because of frequent extrasystoles, sometimes even producing pulsus bigeminus (Fig. 4 Lead I).

The average age at which the slow pulse rate was first observed in our cases was 3.75 years: the youngest was seven months and the

TABLE 1

SUMMARY OF OUR EIGHT CASES

CASE NUMBER	SEX	AGE IN YEARS			HEART RATE AT REST		BLOOD PRESSURE		WASSERMANN REACTION	REMARKS
		WHEN SLOW PULSE FIRST OBSERVED	WHEN FIRST SEEN WITH EKG.	AT PRESENT	AURICLE	VENTRICLE	SYSTOLIC	DIASTOLIC		
1	F	0.6	1.5	3	142-150	50-65	--	--	--	Pulmonary stenosis
2	F	1	12	19	104-120	46-64	160	80	Neg.	
3	M	2	12	13	60-68	43-52	120	65	Neg.	
4	M	2	12	16	136	42-50	120	50	--	Stokes-Adams attacks
5	F	2	27	33	104-112	44-50	190	90	--	
6	M	4	4	6	88-108	39-48	140	65	--	Died
7	F	5	20	21	84-100	46-56	150	90	Neg.	
8	M	13	13	17	75-86	44-56	130	70	Neg.	
Average	--	3.75	12.6	15.7	107	50 45-55	143	73	--	--

oldest thirteen years, but he was the only one who passed his fifth year without attention being drawn to his heart.

The average age at which they first came under our observation and had electrocardiograms taken was 12.6 years. One was eighteen months, one was twenty-seven years, but most of them were about twelve years old.

All the patients are still in good health except one (Case 6), who died when six years old. Two patients (Cases 4 and 5) live too far away to return to the hospital but have replied fully to our enquiries, and all the others have been reexamined this year. Their ages are now thirty-three, twenty-one, nineteen, seventeen, sixteen, thirteen, and three years. Case 2 was fully examined when twelve years old and again when nineteen.

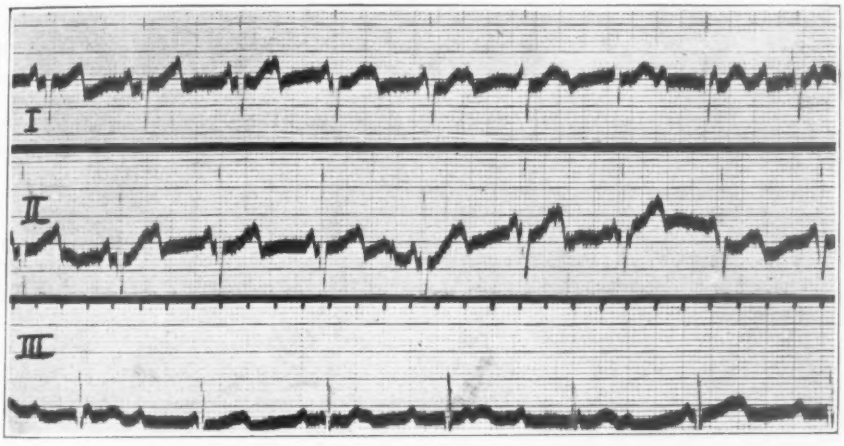

Fig. 1.—Electrocardiogram, Case 1. Complete heart-block: ventricle 75, Lead I; 65, Lead III; auricle, 142. Time marker in this and all other electrocardiograms one-fifth sec.

The first criterion of a slow pulse at an early age was therefore fairly well satisfied, though curiously enough this was never noted during the first few weeks of life. As regards the second, there were physical signs in all 8 cases to suggest congenital heart disease, generally a defect of the interventricular septum. None had morbus caeruleus and only one was diagnosed patent ductus arteriosus and pulmonary stenosis. The third criterion of the absence of infections which might have caused the heart-block was generally observed, and none gave a history of previous diphtheria or rheumatism. Case 6 had acute rheumatism, but this was two years after the heart-block had been diagnosed, and there was nothing to suggest an earlier rheumatic carditis. Stokes-Adams attacks occurred in Case 4 only. The full notes of our 8 cases follow, and certain details are summarized in Table I.

CASE NOTES

CASE 1.—Congenital complete heart-block, patent ductus arteriosus, with some degree of pulmonary stenosis. A slow heart rate and a loud systolic murmur were first noticed when patient was seven months old. When eighteen months old, she was sent to the Heart Hospital from the Infants Hospital, Vincent Square. During five weeks in the hospital her pulse rate had generally been between 50 and 60: as a rule, there had been no symptoms and she had appeared well, but in one or two attacks, perhaps brought on by coughing, her heart rate had risen to 80 and she had been rather cyanosed.

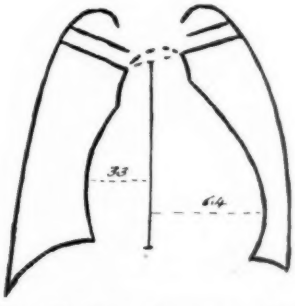

Fig. 2.—Orthodiagram, Case 1. Maximum transverse diameter 9.7 cm. (3.3 plus 6.4) in a chest of 15 cm. Scale reduced to one-quarter.

Fig. 3.—Electrocardiogram, Case 2, on 5, iii, 26. Heart-block probably complete: auricle 136; ventricle 66, or 44 with pulsus bigeminus. Another electrocardiogram of the same date showed no extrasystoles and definite complete heart-block: auricle 116, ventricle 64.

The confinement had been normal. There was no history of any infectious disease. The child appeared normal except for being rather undersized. There was no cyanosis and no clubbing of the fingers. The heart rate after resting was 52; there was complete heart-block. (Fig. 1.) The heart was enlarged to the left, with a forcible apex beat. There was a rough systolic murmur and a thrill, loudest over the pulmonary area. X-ray films confirmed the enlargement to the left and showed some increase to the right also.

When three years old, she was an intelligent child and the picture of health after sunlight treatment. There had been no more attacks of any sort, but she was

not yet able to walk. There was no cyanosis or clubbing of the fingers. The heart rate was 60 and the heart-block was complete, as it had been every time she was seen.

The heart had increased in size since her first examination, and an orthodiagram is shown in Fig. 2 (maximum transverse diameter 9.7 cm. in a chest of 15 cm.). The rough systolic murmur and thrill were most obvious further to the left in the second space, and a diastolic murmur and thrill were present, so that a diagnosis of patent ductus arteriosus could be made. In view of the enlargement of the heart,

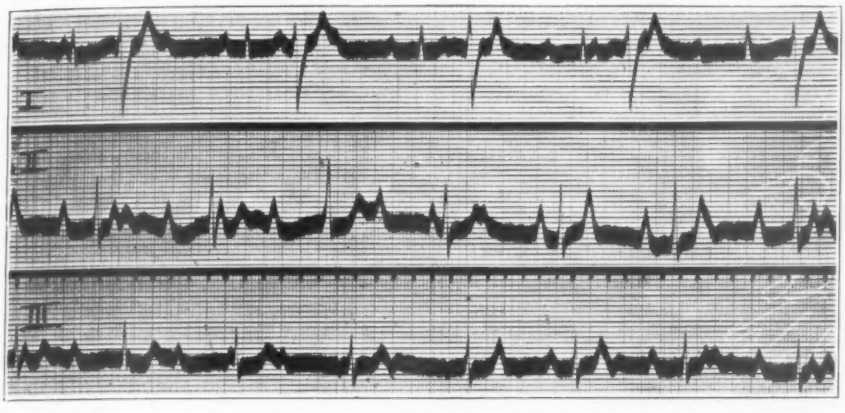

Fig. 4.—Electrocardiogram. Case 2, on 21, xii, 32. Complete heart-block; ventricle 49, Leads II and III; 33 with pulsus bigeminus on Lead I; auricle 104.

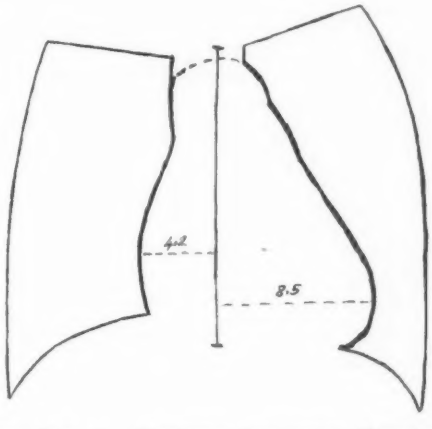

Fig. 5.—Orthodiagram, Case 2. Maximum transverse diameter 12.7 cm. (4.2 plus 8.5) in a chest of 22.8 cm. Scale reduced to one-quarter.

especially to the right, it appeared that there was also some pulmonary stenosis or a large defect of the interventricular septum.

Case 2.—Congenital complete heart-block and patent interventricular septum. At the age of one year congenital heart disease with a slow pulse was diagnosed at a welfare clinic. When twelve years old the patient was first seen at the Heart Hospital. There was no history of rheumatism or any other infections. She looked well and the only symptom complained of was slight breathlessness on exertion, but she had never been allowed to do much in the way of exercise. The apex

beat was beyond the nipple line, diffuse and forcible. There was a systolic murmur, loudest over the pulmonary area and also heard at the apex. No thrill was felt. The heart rate was 64 to 84, this higher figure being due to frequent coupled extrasystoles and complete heart-block (Fig. 3, Lead I).

Seven years later, at the age of nineteen, she looked remarkably healthy. She was working as a shorthand typist, and had kept very well. She walked a good deal, and the only complaint was some dyspnea on running. There was no cyanosis and no clubbing of the fingers.

At first the heart was 52 with some coupling, settling down to 46 with less coupling. The electrocardiogram showed complete heart-block, often with much coupling (Fig. 4, Lead I); there was no obvious change with deep breathing. The apex beat was forcible and beyond the nipple line, and pulsation was felt above the right clavicle and over the pulmonary area. There was a fairly harsh systolic murmur loudest over the pulmonary area and conducted to the apex. The pulmonary second sound was accentuated, and an auricular third sound was often heard. No thrill was felt. X-ray films showed enlargement to the left and right, with a wide

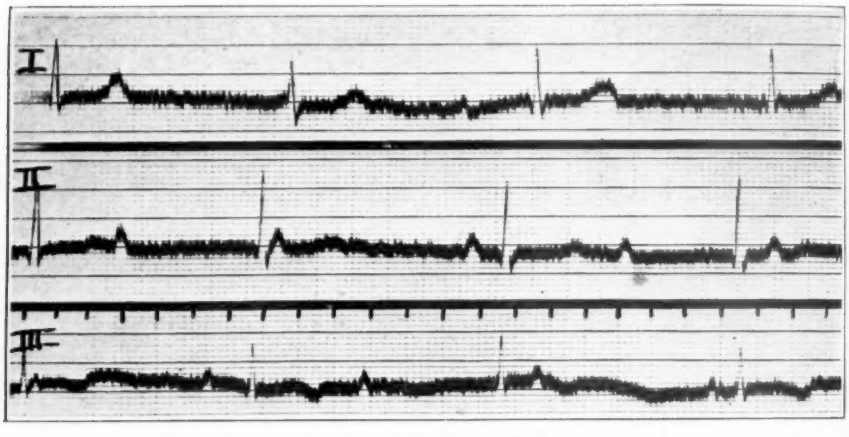

Fig. 6.—Electrocardiogram, Case 3. Complete heart-block: ventricle 43: auricle 61.

pedicle (maximum transverse diameter 12.7 cm. in a chest of 22.8 cm.) (Fig. 5). The conus and pulmonary artery and the aorta were prominent and showed vigorous pulsation. Blood pressure was 160/80. The pulse after exercise rose to 19 in the first quarter minute, dropping to 48 per minute after one minute, thus illustrating the rapid drop to normal.

Seven years after her first electrocardiogram at the hospital and eighteen years after the first observation of her slow pulse, this girl was in good health and almost without symptoms. At sight she would have been taken for a very fit, normal girl.

CASE 3.—Congenital complete heart-block with slight patent interventricular septum. This patient's heart was noticed to be slow at the age of two, when the doctor attended him for bronchitis, and again at the age of three when he had measles. These had been his only illnesses. At six years old, at a routine school examination, a heart murmur was also recorded. He was sent to the Heart Hospital when twelve years old by Dr. J. R. B. Hern; hitherto he had not been allowed to play games at school, but had led a normal life otherwise.

He was a healthy looking boy with no signs of morbus caeruleus. The heart rate varied between 44 and 48 and occasionally 52: it was regular except for an occa-

sional extrasystole. The electrocardiogram (Fig. 6) confirmed complete heart-block. The apex beat was forcible and in the nipple line. An x-ray examination confirmed slight enlargement of the heart to the left (maximum transverse diameter 10.9 cm. in a chest of 20.4 cm.), with a blunt tipped left ventricle: pulsation was well marked in the aorta and in the pulmonary artery, and this was a little fuller than usual. (Fig. 7.) There was a fairly harsh systolic murmur, heard rather widely and best over the precordium. The pulmonary second sound was accentuated and at times reduplicated. No thrill was felt. Blood pressure was 120/65. He was seen again four months later when his condition was unchanged. He had been very liberal in interpreting his permission to take more exercise and had been playing football at school with pleasure and without ill result. It was felt wiser, however, to forbid this until he had been seen for a longer time and his exercise increased more gradually. After another four months he was getting on well and still anxious to be allowed to play all games at school.

CASE 4.—Congenital complete heart-block with some patency of the interventricular septum. He was the only patient in this series with Stokes-Adams attacks. At the age of two years he was playing on the sands when he had a fit in which he went

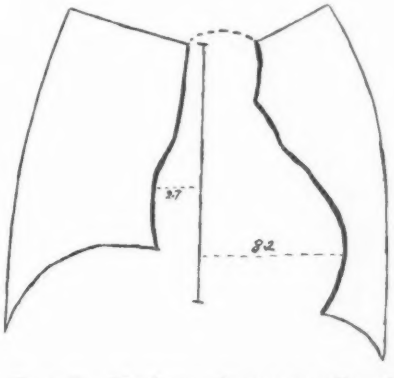

Fig. 7.—Orthodiagram, Case 3. Maximum transverse diameter 10.9 cm. (2.7 plus 8.2) in a chest of 20.4 cm. Scale reduced to one-quarter.

stiff and blue. For two years he had these attacks rather frequently, sometimes as many as three a week, but otherwise remained quite well. Unfortunately the doctor who attended him then is dead, but the patient's mother remembers his saying it was due to his heart which was always slow; i.e., in between the attacks when he appeared quite well.

During the next eight years he was much better and had only four attacks. His mother described the last one as follows: After a sudden groan he went unconscious; he was stiff and blue with no movements of any sort; she thought that he was unconscious for twenty minutes; afterward he apparently recovered very quickly. Except for these attacks he had no complaints. There was no history of rheumatism or of any infectious diseases. He was sent to Guy's Hospital by Dr. C. A. Hicks, when twelve years old.

He appeared to be a healthy boy. His heart rate at rest was generally about 42, with at times fairly frequent extrasystoles; and an electrocardiogram (Fig. 8) confirmed complete heart-block. The heart was slightly, if at all, enlarged (no x-ray examination was made). There was a systolic murmur best heard in the fourth, fifth, and sixth spaces to the left of the sternum. No thrill was recorded. Blood pressure was 120/45.

Because of the distance from London it has not been possible to get him up to the hospital again, but he has remained well, leading a normal life with no more attacks. He is now sixteen years old, and his heart rate remains slow.

CASE 5.—Congenital complete heart-block, and patent interventricular septum. Her slow pulse was first noted by her doctor when she was two years old. She attended the Heart Hospital under the care of Dr. Parkinson when twenty-seven years old. Until a year before she had always been very fit and had been able to cycle

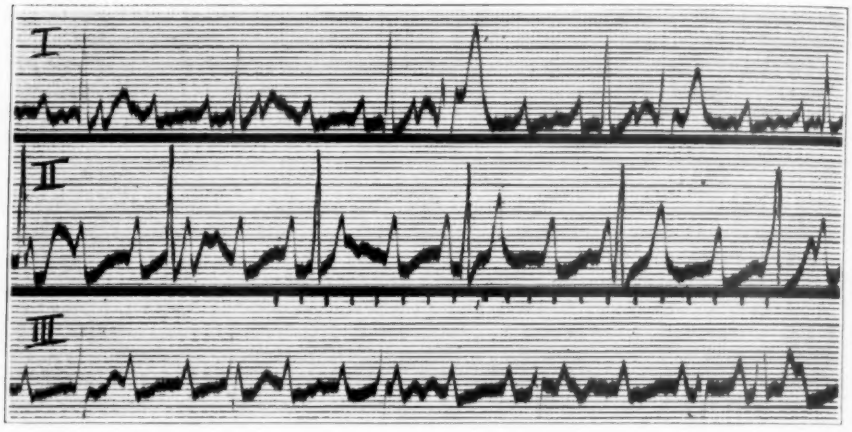

Fig. 8.—Electrocardiogram, Case 4. Complete heart-block: ventricle 50, or 35 with pulsus bigeminus; auricle 144. The P-waves were large in all the electrocardiograms taken in 1929, but he has not had one taken since.

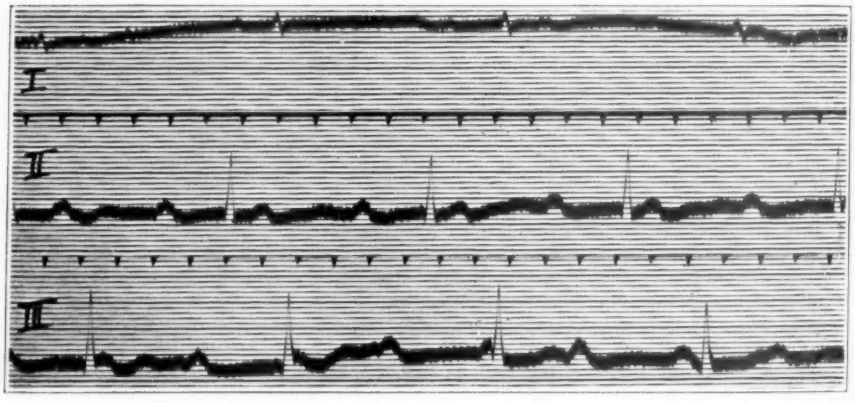

Fig. 9.—Electrocardiogram, Case 5. Complete heart-block: ventricle 52; auricle 113. Slow pulse was noticed at age of two years; patient is now thirty-three years old. In Lead II the degree of block is probably complete though the ventricular is nearly half the auricular rate.

forty miles in a day. Recently, she had been coughing and had become a little tired and short of breath, and had also lost some weight. She gave no history of rheumatic fever.

She looked well, with no signs of morbus caeruleus. Her pulse rate was between 46 and 50, and there was complete heart-block. (Fig. 9.) The heart was a little enlarged to the left, and the conus showed rather prominent pulsation. There was a systolic murmur at the apex without any thrill. Blood pressure was 190/90. No evidence of tuberculosis was found. She attended the hospital for about six months.

Now, six years later, at the age of thirty-three, she is keeping in good health, able to do ordinary housework on a farm, and to walk two miles a day. It has not been possible to examine her again, but the pulse rate is still slow.

CASE 6.—Congenital morbus cordis with complete heart-block. Death from rheumatic carditis. Patient was admitted to the Heart Hospital under Doctor Parkinson from the Fever Hospital when four years old. A slow pulse of 42 had been noticed before his attack of scarlet fever, and during the pyrexial phase it had been only 52. There was no history of rheumatism or of other illnesses.

His appearance was that of a healthy boy, and there were no outward signs of congenital heart disease, and no cardiac symptoms. There was complete heart-block and the rate varied between 32 and 48 (Fig. 10); on one occasion this faster rate was produced by atropine, but at other times it was as fast as this spontaneously. The heart was enlarged to the left; there was a forcible apex beat and a loud systolic murmur chiefly at the apex. There was no thrill. Blood pressure was 140/65.

Fig. 10.—Electrocardiogram, Case 6. Complete heart-block: ventricle 39; auricle 88.

He progressed fairly well for eighteen months, his heart rate being from 45 to 50. He was then admitted to the University College Hospital with pyrexia and painful and swollen joints, and his condition was diagnosed as congenital heart disease with subsequent rheumatic complications. Complete heart-block was again confirmed. There was no evidence of infective endocarditis. He died after two weeks, but, unfortunately, an autopsy was refused.

CASE 7.—Complete congenital heart-block with patent interventricular septum. This patient had been told that her heart was affected and that she had a slow pulse when five years old. There was no history of rheumatic fever or of any infectious diseases. She was sent to the Heart Hospital by Dr. Baron when she was twenty, complaining of feeling tired and of attacks of giddiness and faintness during the last few months. These had been occurring about once a month and sometimes she had lost consciousness. She had not been allowed to play games at school and was somewhat breathless on any special exertion. She was leading a normal life, working as a hair-dresser.

She appeared to be a healthy girl, with no signs of morbus caeruleus. Her heart rate was regular at 52, falling to 44 after she had been resting. An electro-

cardiogram confirmed the diagnosis of complete heart-block (Fig. 11). With exercise the heart quickened, being at the rate of 60 in the first quarter minute afterward.

The apex beat was forcible and just outside the nipple line. From time to time it was specially forcible and at the same time the carotid pulsation was increased. X-ray films confirmed slight enlargement to the left (maximum transverse diameter 11.7 cm. in a chest of 23.2 cm.; Fig. 12). The conus was prominent, and this and

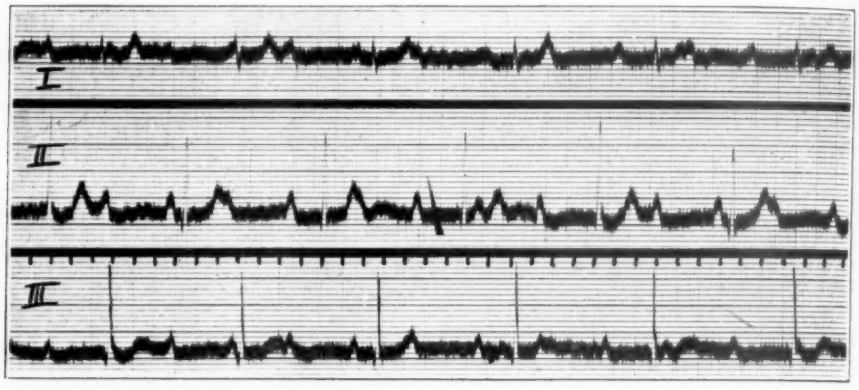

Fig. 11.—Electrocardiogram, Case 7. Complete heart-block: ventricle 46, auricle 100.

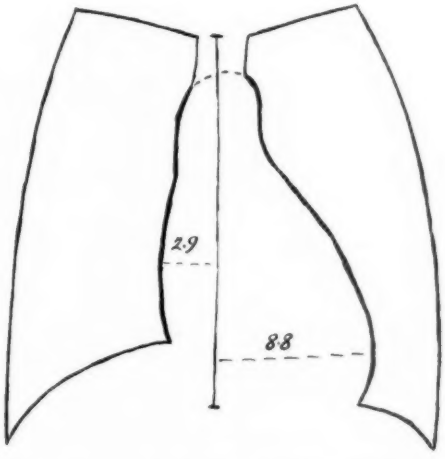

Fig. 12.—Orthodiagram, Case 7. Maximum transverse diameter 11.7 cm. (2.9 plus 8.8) in a chest 23.2 cm. Scale reduced to one-quarter.

the aortic knob and the heart itself showed vary vigorous pulsation. There was a systolic murmur best heard inside the apex, and a systolic thrill in the same site. Auricular sounds were frequently heard. Blood pressure was 160/80.

The attacks of faintness and giddiness were regarded as ordinary faints and not as Stokes-Adams attacks, and this was confirmed by their disappearance with treatment—an iron tonic and reassurance—and by their occurrence under emotional stress. On two occasions when a period of faintness was observed, the pulse rate rose to 60 and was of poor volume; she was not unconscious, and as she recovered, the volume of the pulse improved and the rate fell to 44.

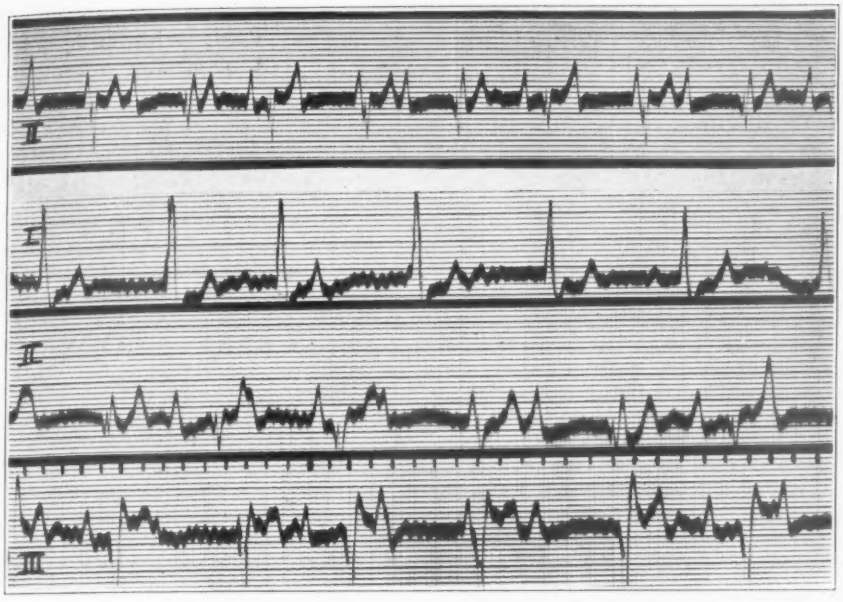

Fig. 13.—Electrocardiogram, Case 8. Complete heart-block: ventricle 51, auricle 86.

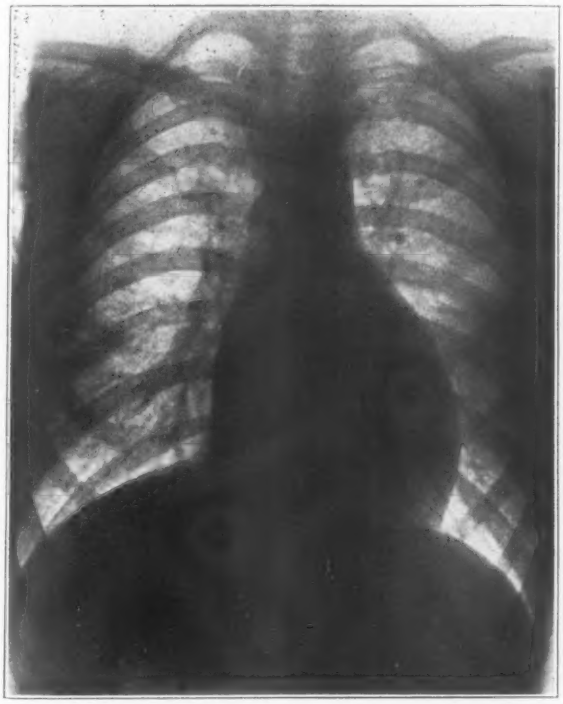

Fig. 14.—Teleradiogram, Case 8. Heart appears rather rounded and prominent to the right and in the pulmonary arc. Maximum transverse diameter 13.9 cm.

She has now been under observation for two years and has lost most of her symptoms and returned to work. Most often her heart rate on arrival in the room has been about 52, falling after she has been sitting for some minutes to 44 or 46. Sometimes it was 54 or 56, and did not always show much tendency to settle quickly to the slow rate.

CASE 8.—Congenital complete heart-block; slight patent interventricular septum. This patient was first told he had heart disease by the school doctor when he was thirteen years old, and was sent to Guy's Hospital. He gave no history of rheumatic fever or of diphtheria. He complained of no symptoms but was small for his age.

His heart rate was 54 and regular, with complete heart-block (Fig. 13). He had a systolic murmur beat heard in the pulmonary area and conducted to the apex. No thrill was felt. His heart was enlarged to the left, and the apex beat was forcible. Blood pressure was 130/70. His pulse rose to 63 after exercise.

When seen two years later, his heart rate was 52, rising to 60 after exercise. After another two years, when he was seventeen, he felt well and was working in a bottling factory. He was still small, but complained of nothing except that he was rather short of breath when playing footfall. The heart rate was 44 and fell to 40 after resting. The physical signs were unchanged. X-ray films confirmed the enlargement of the heart, mainly to the left (Fig. 14).

THE HEART RATE AT REST

The rate at rest generally varied between 42 and 56 and the average was 50. It may be because of this relatively fast rate that the diagnosis is not made more frequently. It was unusual to find a rate under 40, though Fig. 6 shows a rate of 38. Table II shows the slowest ventricular rate observed in our 8 and in 38 of the 45 collected cases; in the remaining 7 the block was not complete. In addition to the 30 cases collected by Yater[29] and our own 8, single cases have been reported by Anderson[4] Koenen,[14] Brandenberg,[6] Godfrey and Palmer,[12] Leech,[15] Nicholson,[19] Selar,[22] Sprague and White,[24] and Wood and Rogers.[28] Recently Aitken[1] reported two cases of her own and added one reported by Calandre[7] and two reported by Aylward,[5] where an electrocardiogram has since been obtained. This with the specimen of Moxon[18] makes a total of 53 cases and these are the ones referred to subsequently as collected cases.

TABLE II

SLOWEST VENTRICULAR RATE IN CONGENITAL COMPLETE HEART-BLOCK

Ventricular rate	20-29	30-39	40-44	45-49	50-54	55-59	60 and over
Number of cases	2	5	15	12	5	3	4

The rate may be much faster than this; most of our patients at times had rates of over 50 when at rest. A ventricular rate of 75 was recorded in an infant (Lead I Fig. 1); and a rate of 64 was recorded in Case 2 when the patient was twelve years old. Faster rates were noted after exercise. Although this is such a contrast to the rates found in elderly patients with degenerative changes and complete heart-block, it is not

confined to the congenital group, for sometimes rates much faster than these have been observed in complete heart-block during diphtheria.

The auricular rate was also rather fast, averaging 107; in four patients it was never noted under 100, but possibly it would have been if they had rested longer before the electrocardiograms were taken.

The Blood Pressure.—In the three elder patients this was higher than might be expected—160/80, 190/90, and 150/90 at ages nineteen, twenty-seven, and twenty-one, respectively (Cases 2, 5, and 7). In the remainder the figures were normal (Table I). There was no renal disease and no evidence of any arterial change, and probably the rise is a reaction to maintain a normal pressure during the prolonged diastolic period.

THE EFFECT OF EXERCISE ON THE HEART RATE

The ventricular rate generally returns to its normal rather quickly after exercise. It is therefore easy to miss the maximum rise, which may be quite high if the rate is taken for a short period, such as fifteen seconds. The results in four patients are shown in Table III. Except in Case 2 the fall was so rapid that the rise for a whole minute was not much, though the increase during the first fifteen seconds was considerable, all rising to 60 or over. Aitken[1] mentions rates of 57 and 58 in her two cases, and Fleming and Stevenson[11] also noted a rise from 49 to 68 after exercise.

TABLE III

PULSE RATE AFTER EXERCISE

	AT REST	AFTER EXERCISE				
		QUARTER MINUTE				FIRST MINUTE
		1	2	3	4	
Case 2 (a)	46	17	15	13	12	57
(b)	46	19	15	13	12	59*
Case 3 (a)	48	14	13	12	12	51
(b)	46	15	13	12	12	52*
Case 7	48	15	14	12	11	52
Case 8	56	16	16	16	15	63*

*Three minute exercise; others were for shorter periods.

In Case 3 this was confirmed by taking an electrocardiogram as soon as possible, and then, though a rather longer interval elapsed while the patient was lying down and the instrument being adjusted, a ventricular rate of 56 was recorded, where it had been 46 just before. On this occasion the auricular rate could also be measured, and it was 97 instead of his usual 60 to 68; i.e., the auricular rate had increased just as much as one would expect after exercise in a normal person, and the ventricular rate had increased, though not to the same extent. It seems most likely that the chemical changes in the blood, especially the increased CO_2 content, are responsible for the increase of rate.

In ordinary cases of heart-block the rise in ventricular rate with exercise is less than this, but occasionally it is even more. In one of our patients in whom the rate at rest was generally 42 to 50, it rose to 70 after exercise.

Liljestrand and Zander[16] have investigated one case very thoroughly, and their work is useful in understanding the circulation in heart-block. He was a young man of twenty who was able to take part in strenuous games, and to swim "for as long as he liked." When three years old he had pneumonia and was found to have an irregular pulse. After that, he was liable to fainting attacks, and when five years old, he was sent to the hospital where he was found to have a ventricular rate of 45 to 50 and complete heart-block. He had steadily improved from then on and had lost any tendency to fainting attacks. It is possible that the block was congenital and not due to his pneumonia. His ventricular rate increased up to over 100 with strenuous exercise.

The minute volume of his circulation was about normal, but on one occasion when the rate was 37 the output per beat was 123 c.c. (i.e., minute volume 4.5 liters) compared with a normal when the rate was 70 with an output per beat of 70 c.c. (i.e., minute volume 4.9 liters). With violent exercise the minute volume was increased to 16.4 liters (ventricular rate 94 with an output per beat of 174 c.c.): a control taking the same exercise increased his minute volume to 19.8 liters (ventricular rate 140 with an output per beat of 140 c.c.). Lundsgaard[17] also found the output per beat raised to about 150 c.c. in complete heart-block. This increased output per beat is associated with the forcible beat of the ventricle to be seen when many of these patients are x-rayed. It explains why they have no undue dyspnea with moderate exertion, in spite of their slow heart rate.

THE EFFECT OF ATROPINE ON THE HEART RATE

In two of our cases observations were made after injection of atropine. In Case 3 1/150 gr. did not increase the auricular rate above 70 (thirty-five minutes) or the ventricular above 49 (forty minutes), 60 and 45 being the rates at rest that morning for the auricle and ventricle, respectively. In Case 7 1/150 gr. raised the auricular rate to 120 from 77 and the ventricular rate to 56 from 44 after forty minutes.

Aitken[1] has collected 12 cases in which the effect of atropine was observed. Auriculoventricular dissociation was never restored, and she rightly adduces this as showing that the vagus is not the cause of the block. Both auricular and ventricular rates were considerably increased, in four, but in two the auricle was faster and the ventricle was unchanged. Atropine was without effect on either, in the remaining six; so possibly the dose was insufficient. In Leech's case[15] the ventricle increased from 47 to 79 in twenty minutes, but generally the greatest effect was

noted in about thirty-five to forty minutes—94 from 62, and 83 from 55 in Aitken's two cases, and 78 from 56 in one of Fleming's cases.[11]

THE EFFECT OF FAINTNESS ON THE HEART RATE

The main complaint for which one patient (Case 7) came to the hospital was faintness, and we were fortunate in observing this twice. We had already formed the opinion that the faints were of vagal origin

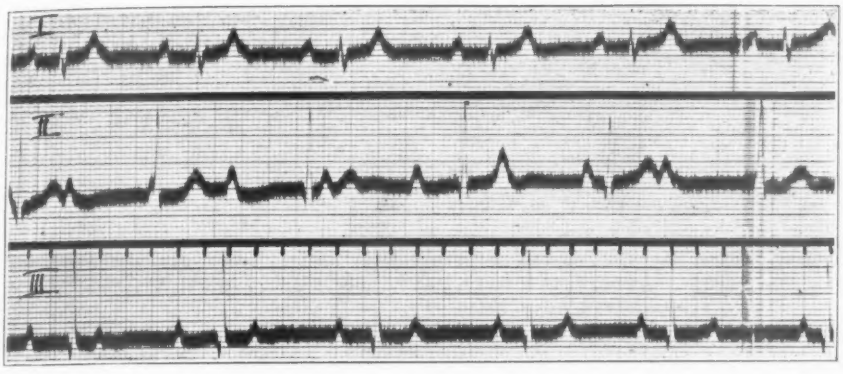

Fig. 15.—Electrocardiogram, Case 7, just after the onset of faintness, forty minutes after atropine had been given. Lead I: ventricle 53, auricle 107; Lead II: ventricle 52, auricle 92; Lead III: ventricle 50, auricle 99.

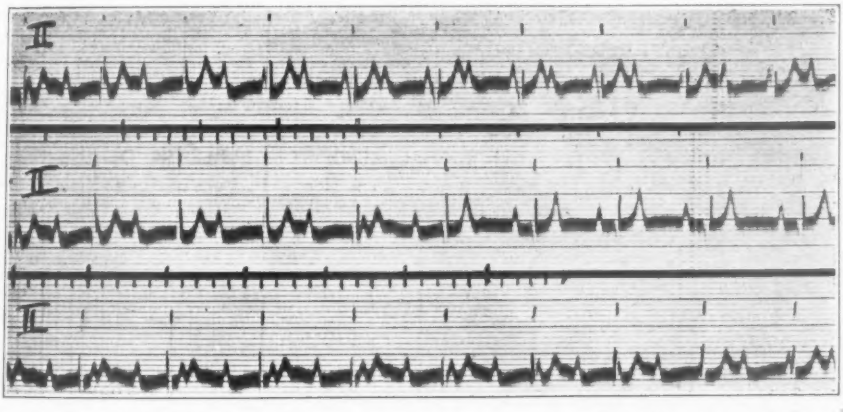

Fig. 16.—Electrocardiogram, Case 7, taken three minutes after Fig. 15, during an attack of faintness. Lead II only: ventricle 56 to 51, auricle 112 to 109.

and not Stokes-Adams attacks, from the general description, from their recent onset, and from the effect of emotion. This view was confirmed by their disappearance with treatment and by her return to work.

On one occasion atropine had been injected forty minutes before, and no doubt she was tired with repeated examinations and electrocardiograms. Just before Fig. 15 was taken, she complained of "a funny feeling in the stomach." Three minutes later while still sitting in the chair she "fainted." She was pale and there was no cyanosis. She was

not unconscious. Her pulse rate was 60, and no period of a slow pulse was noted, although she was under almost continuous observation. This is in contrast to the ordinary faint where the weak rapid pulse comes later, and where at the beginning the pulse is slow and sometimes not quite regular. Fig. 16 was taken during the attack which lasted about five minutes. In ten minutes she felt well and was able to walk home. The other observed attack was very similar.

ASSOCIATED CONGENITAL LESIONS

In most of the reported cases there has been some degree of cardiac enlargement, but generally it has been slight or moderate, as was true in our 8 cases. It is often easy to say that a patient has congenital heart disease but more difficult to decide exactly what the congenital abnormality is. None of our 8 cases had obvious cyanosis or clubbed fingers or the complete picture of morbus caeruleus. All had signs which suggested that there was a patent interventricular septum, and one patient probably had some degree of pulmonary stenosis.

This agrees with most other reports of congenital heart-block. Of our 8 and the 45 collected cases 8 (15 per cent) had obvious cyanosis at rest, generally with clubbed fingers; in these there was gross congenital heart disease, most often pulmonary stenosis with other associated lesions.

Apart from this 15 per cent, another 35 (67 per cent) had signs of a patent interventricular septum. In the remainder the signs were too slight to make a definite diagnosis, but there were only three or four in which the authors found no signs to suggest structural congenital disease of slight degree. Among this group with patent interventricular septum there were 13 (25 per cent) with some degree of cyanosis, though often it was only slight or only present on exertion. There were also the 8 with more obvious cyanosis at rest, but this still leaves more than half (60 per cent) in whom no cyanosis was observed.

CASES WITH POSTMORTEM EXAMINATION

We have found published reports of only three cases and add a fourth of a specimen, so far as we know not published previously.

I. Moxon's case (Guy's Hospital Museum. Specimen 2317.).—A boy, aged two years, with extreme cyanosis and dyspnea, was admitted under Dr. Moxon in 1879. The second sound was greatly accentuated in the pulmonary area and the pulse rate was 25 a minute. He was apparently well until he was a year old, when, after having whooping cough, he began to be cyanosed. This became much worse seven months before his admission. He died suddenly after he had been in the hospital a month.

The pulmonary artery was completely occluded at its origin and was only a small tube up to the entrance of the patent ductus arteriosus, where it became of normal size. There was a large opening in the upper

part of the interventricular septum, and the right ventricle was greatly hypertrophied, the wall being thicker than that of the left. Except for the condition of the heart the other viscera were normal.

The slow pulse and the cyanosis were not noted until after his whooping cough, but in view of the condition of the heart it is certain that the lesion was congenital and therefore it is probable that the slow pulse was also congenital, the illness having made his condition much more noticeable. Only one other case has been recorded with such a slow pulse rate (D'Espine and Cottin[10]), but it is difficult to think of any diagnosis but complete heart-block. The earliest generally accepted case is that of van den Heuval in 1908.[25]

II. Wilson and Grant's Case.[27]—A child of fourteen months with incomplete heart-block. Examination showed complete stenosis of the pulmonary artery with a large patent ductus arteriosus and a common ventricle with only the rudiment of an interventricular septum in the form of a rounded muscular prominence on the posterior wall. Histologically, the auriculoventricular node was well developed, and situated in the interauricular septum and the central fibrous body. But the fibers coming from it were interrupted and broken up by the fibrous tissue of the central fibrous body. The fibers ultimately reunited, however, and divided normally into right and left branches.

III. Perotti's case.[20]—A child three days old, in whom examination showed complete absence of the membranous portion of the interventricular septum. Histologic examination was not made.

IV. Yater's case.[29]—A child a few days old, in whom examination showed transposition of all the viscera and great vessels, except the ventricles of the heart. The ductus arteriosus was patent, and there was a patent foramen ovale and a small patency in the interventricular septum. The sino-auricular node was found in the wall of the auricle one the left side (structurally this corresponded with the right auricle). The auriculoventricular node lay against the right side of the central fibrous body in the auricle of the right side. The node was separated into two parts by fibrous tissue from the central fibrous body, thus separating the A-V node from the bundle of His.

PROGNOSIS

As few of the patients described have been over twenty years of age and as none seems to have been older than our patient (Case 5), it might seem that the outlook is good for a time but that few survive long in adult life. Probably this is incorrect and when patients have been followed for a longer time they may be found in good health at a more advanced age. They may not have been reported at older ages because the possibility of the block being congenital has not been considered.

In some cases, especially in patients who have died in the first few weeks of life, the associated malformation of the heart and not the heart-block was the cause of death. Stokes-Adams attacks increase the risk of sudden death, but they are found in a small minority only and the risk is less than might be expected.

Nine of the 53 patients are known to be dead. Four died in early infancy, probably because of the associated congenital malformations. Our patient (Case 6) died of infective endocarditis, an added complication of his congenital heart, and the block was probably without significance. The remaining four died suddenly. The first, whose sister also has congenital heart-block, had a patent interventricular septum and occasional attacks of cyanosis; at three months old the pulse became irregular and she died in one of these attacks.[5] The second died suddenly at two years, having had gross cyanosis and dyspnea for some time.[18] The third had extreme cyanosis and pulmonary stenosis and died suddenly at the age of nine years.[23] All these three had serious congenital heart disease as well as block and are mentioned here only because of the suddenness of their deaths. Were it not for the next case, one might feel that the prognosis was excellent as regards the heart-block and need be considered only as regards the associated malformation. The fourth had no other signs of heart disease and no symptoms, and was accustomed to bathing and strenuous exercise, but she died suddenly when thirteen years old just as she was going into the water.[2] In her, at any rate, a fatal Stokes-Adams attack seems the likely explanation, but curiously enough none of these four gave a history of syncopal attacks, though these were present in 8 other patients, all, so far as we know, still alive.

CONCLUSIONS

Congenital heart-block is probably more common than has been thought, and this possibility should be remembered when treating children with a slow pulse. The block is more often complete than partial.

The ventricular rate is usually between 42 and 56 and quickens to 60 or faster with exercise. Stokes-Adams attacks are not common but occur in about one-eighth of the patients, generally in the first few years of life.

As a rule, there is some degree of patency of the interventricular septum, and the heart is a little enlarged, often to both sides, with marked pulsation and some prominence of the pulmonary arc. More serious abnormalities and typical morbus caeruleus are less common.

Provided that the associated malformation is not in itself serious, the outlook is good. Sudden death is a rare catastrophe. Usually, the subject is able to lead an active life with little or no dyspnea, and survives to adult life or much longer.

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RUPTURE OF THE RIGHT AURICLE OF THE HEART*

Case Report With Electrocardiographic and Post-Mortem Findings

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INTRODUCTION

OUR knowledge of rupture of the heart dates from the time of Harvey[1] who in 1647 described the first case, since which report there have been numerous contributions to the subject, dealing for the most part with ventricular rupture. The frequency of this finding at post-mortem examination is apparently increasing. There are found wide variations in the incidence of cardiac rupture according to the statistics which are consulted. Thus the older figures cited by Krumbhaar and Crowell[2] are as follows: Philadelphia General Hospital, 7 cases in 16,000 autopsies; and Romeik of Munich, 7 cases in 13,000 autopsies. More recently De la Chapelle[3] has reported 20 cases among 15,000 autopsies performed by the medical examiner's service in New York City, while Benson, Hunter and Manlove[4] record 40 ruptures among nearly 7,000 autopsies. The records of 1,454 consecutive post-mortem examinations at the Albany Hospital contain 6 instances of cardiac rupture.

Krumbhaar and Crowell[2] in 1925, and Davenport[5] in 1928 in a supplementary analysis, have made a most exhaustive statistical study of all the cases of cardiac rupture in the literature from 1872 to 1928. In a grand total of 710 cases they found the site of the rupture distributed as follows: left ventricle 566 (79.8 per cent), right ventricle 76 (10.7 per cent); right auricle 38 (5.3 per cent), left auricle 13 (1.8 per cent), and miscellaneous 17 (2.4 per cent).

It is well known that cardiac rupture is an accident chiefly confined to the left ventricle, and that it occurs principally in the advanced years of life—the decades from fifty to eighty years. Furthermore it is practically always secondary to cardiac infarction, the result of coronary artery occlusion, by either thrombosis or fibrotic narrowing. It is indeed doubtful whether a perfectly healthy heart is ever spontaneously ruptured, as signs of pre-existing disease can usually be found.

The facts known about rupture of the auricle are fewer and less clearly defined than those pertaining to the ventricle. Rupture of the

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auricle is a rare but not by any means unique condition. In the series referred to above there was a total of 51 cases, or 7 per cent, and the right auricle was affected three times as frequently as the left. A review of the literature reveals that most of the communications contain but brief clinical and pathological notes. No case has thus far been reported in which serial electrocardiograms were taken immediately following the onset of symptoms.* Microscopic examination of the ruptured auricular wall has been made in only a small percentage of the cases described. The following case with serial electrocardiographic observations and histological study is therefore considered worthy of record:

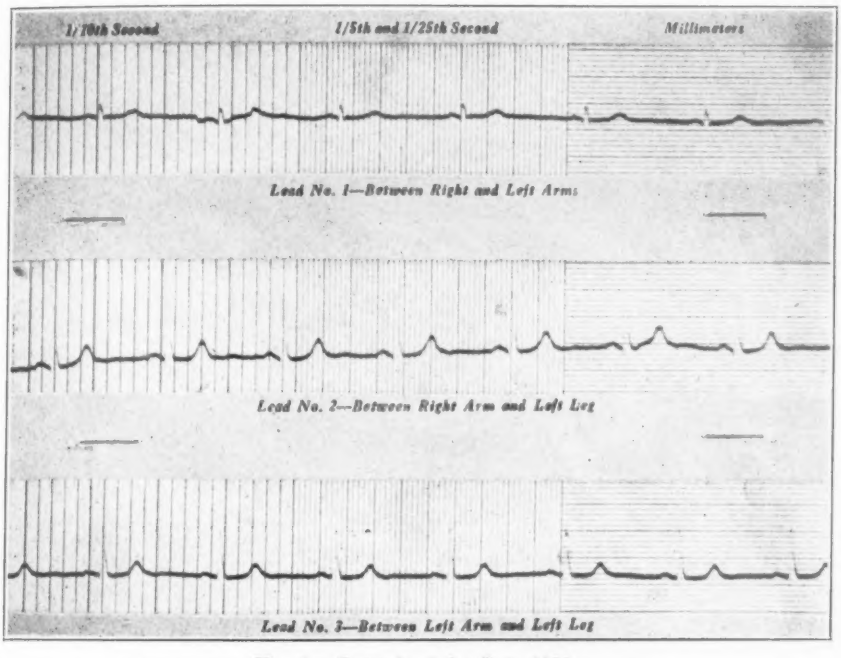

1/10th Second
1/5th and 1/25th Second
Millimeters
Lead No. 1—Between Right and Left Arms
Lead No. 2—Between Right Arm and Left Leg
Lead No. 3—Between Left Arm and Left Leg

Fig. 1.—Record of April 4, 1930.

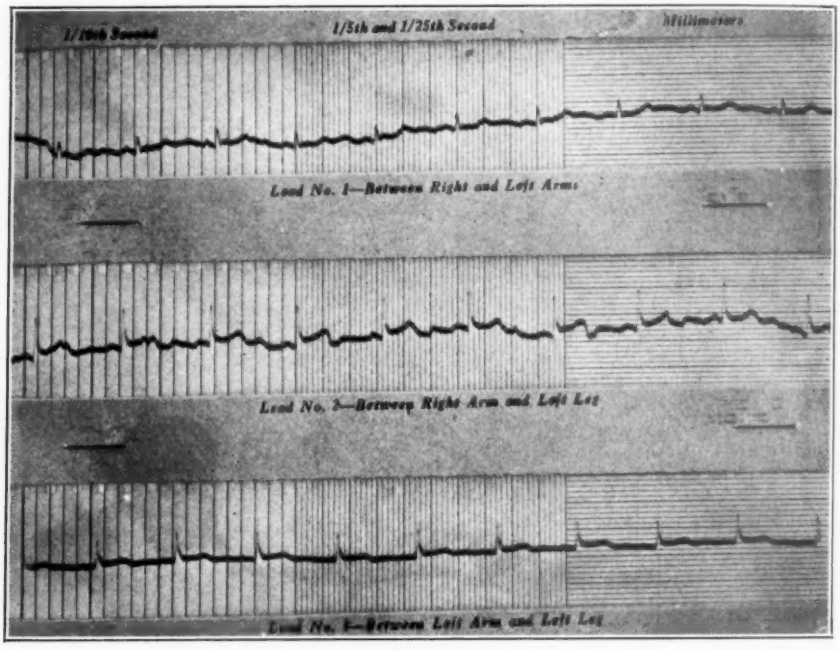
CASE REPORT

The patient, an electrical engineer, forty-three years of age, married, with two healthy children, had always enjoyed excellent health. There was no history of preceding cardiac disease or of syphilis. On the evening of April 3, 1930, while rubbing himself with a towel after a bath, he was suddenly seized with excruciating substernal pain which radiated to the neck and head. He fell to the floor unconscious but after about fifteen minutes revived, vomited, and helped himself to bed. The pain persisted during the night, in the chest, head and back of the neck. His physician, summoned the following morning, found the patient, a sparely nourished, well-developed man, looking pale and ill but not dyspneic—the pain subsiding—temperature 100° F., pulse 80, regular, good quality in the right wrist, but not

*Lisa and Ring[6] have published two electrocardiographic tracings taken two years and one month respectively before death. Their case showed an infarct of the left ventricle, as well as rupture of the left auricle.

detectable in the left. The heart was normal in size and outline, its action regular, and a soft systolic murmur was heard over the aortic area, transmitted to the right side of the neck. There was no pericardial friction rub. Blood pressure in the right arm was 150/50 mm., in the left a few beats came through at 60 mm., but the diastolic pressure could not be determined. There were no color changes or disturbances of sensation in the two hands. Physical examination was otherwise entirely negative.

During the next three days the patient's condition did not change essentially. Slight fever continued, the pulse ranged from 80 to 100; the pain had diminished to the level of a substernal soreness; the systolic murmur disappeared; no cardiac friction developed, and the inequality of blood pressure in the two arms persisted. On April 7, following an examination in which an enfeeblement of the heart sounds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Millimeters
Lead No. 1—Between Right and Left Arms
Lead No. 2—Between Right Arm and Left Leg
Lead No. 3—Between Left Arm and Left Leg

Fig. 2.—Record of April 6, 1930.

and slight dullness at the bases of the lungs with a few fine râles were noted, the patient suddenly made several convulsive movements, the face became livid, the pulse disappeared from the right wrist, and death ensued at once.

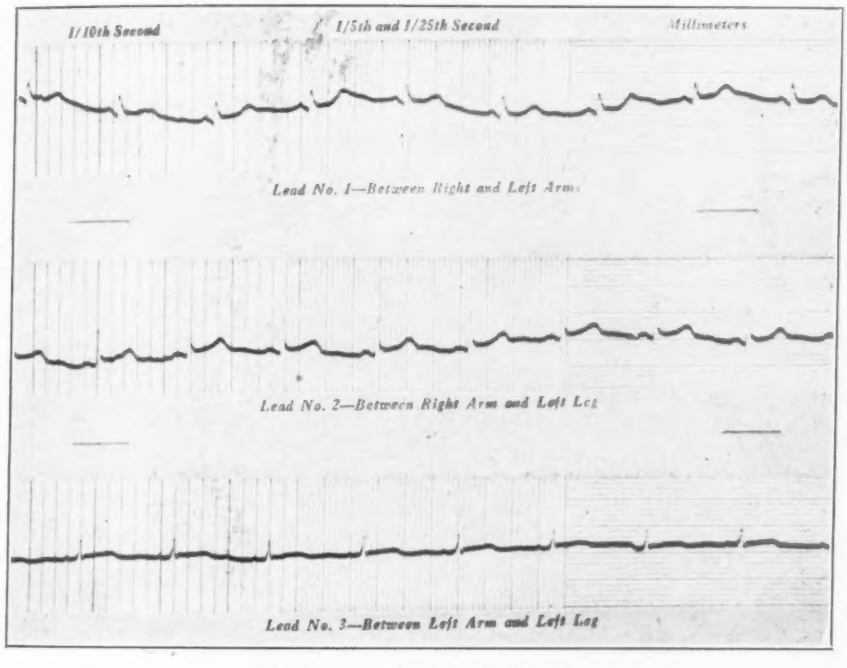
Laboratory Data.—Leucocyte count 9,800; polymorphonuclears 67 per cent, lymphocytes 30 per cent, monocytes 2 per cent, eosinophiles 1 per cent. Red cells normal. Urine examination negative. Blood Wassermann reaction negative. Electrocardiograms were taken on April 4, 6, and 7 (Figs. 1, 2, and 3).

Fig. 1. Record of April 4, 1930. Rhythm regular. Rate 65-70. A-V conduction normal. QRS width within normal. S-T time normal. P-waves practically normal; possibly a little widened. R_1 is low; R_2 is normal in height but slurred and widened to nearly 0.08 sec. R_3 is slightly lower than R_2 and also slurred and widened a little. S-waves absent. T-waves normal.

Diagnosis.—A slight delay in intraventricular conduction is indicated by Leads II and III.

Fig. 2. Record of April 6, 1930. Rhythm regular. Rate about 100. A-V conduction normal. QRS width normal in Lead I but increased in Leads II and III, owing to the elevated take-off of the S-T line. S-T time not measurable owing to the deformity of T. The P-waves show no significant change. R_1 is unchanged. R_2 is lower than on April 4, as is R_3 also. S-waves absent. A change in the S-T line has occurred. In Lead I it is convex upward and in Lead II it is reversed, concave, and takes off well above the P-R level. In Lead II S-T is horizontal but takes off a little above the P-R level. The form of T is variable in Leads I and II especially and in those leads there is an extra wave of variable shape and height after the T-wave.

Diagnosis.—The cardiogram strongly suggests a coronary occlusion. In any event, some myocardial injury has occurred.


1/10th Second
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Millimeters
Lead No. 1—Between Right and Left Arms
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Fig. 3.—Record of April 7, 1930.

Fig. 3. Record of April 7, 1930. Rhythm regular. Rate about 85. A-V conduction normal. The QRS (actually only the R) width has increased in Lead I since April 6, and decreased somewhat in Leads II and III. S-T time not measurable. There are slight changes in the P-waves. R_1 is widened since yesterday and the S-T line is now concave and takes off above the P-R (isoelectric) level. R_2 is unchanged. The S-T line of Lead II still takes off above the P-R level. R_3 is lower than on yesterday. T_1 is higher than it has been on the two previous days and is variable in form. T_2 is less variable than on yesterday. The extra wave after it is inconspicuous today.

Diagnosis.—Unchanged (see report of April 6). In summary one may say that the various changes described in the QRST complex indicate a suddenly developing disturbance of the ventricular musculature, and they further suggest a decline in myocardial efficiency, due possibly to a coronary occlusion. (Since a calibration

curve is not given for the record of April 6, too much importance should not be given the comparisons of wave amplitude.)

Portable x-ray film of chest taken April 7, 1930, the day before death, showed diminished transmission of rays through the lower right chest. The heart is apparently enlarged, and the shadow of the great vessels measures 9.3 cm. This change cannot be considered as of diagnostic value, because the plate was taken with the patient lying in bed, and not at six feet; hence a certain amount of distortion must have occurred. A slight prominence of the shadow in the region of the right auricle is noted.

Fig. 4.—Photograph of heart. Reconstruction after dissection. Note line of rupture in right auricle.

Diagnosis.—A positive clinical diagnosis was not made. In favor of coronary occlusion were the history of long-continued severe substernal pain, with fever, and suggestive electrocardiographic changes. The differences in blood pressure on the two sides and the probable increase in the mediastinal shadow suggested the tentative diagnosis of vascular accident with infiltration of the mediastinal tissues, perhaps due to rupture of a dissecting aneurysm.

Post-Mortem Examination.—Necropsy was strictly limited to examination of the heart in which the following changes were observed:

On opening the pericardial sac, the cavity was found to contain approximately 500 c.c. of soft, dark red, freshly clotted blood. After removal of the clot, the lining surfaces appeared roughened owing to the presence of a fine deposit of fibrin. The

heart weighed 300 grams. The epicardium was blood stained. None of the cavities was dilated. An increased amount of epicardial fat was present, particularly about the right ventricle. The right auricle appeared quite fibrous and hemorrhagic. On the anterior surface of the auricle toward the right border a somewhat S-shaped tear 2 cm. long was found, the margins of which were blood stained. The tear involved the entire thickness of the auricular wall, and a small amount of clot protruded through the opening. This area and the adjoining portion of the auricular wall were very thin and hemorrhagic, as though infiltrated by blood. (Fig. 4.) On the posterior aspect of the auricle was a large, thick, grayish, fibrous patch. The left auricle was comparatively normal. The tissues at the base of the heart were infiltrated by blood. Examined in situ, the mitral and tricuspid valves appeared normal. The aortic cusps were rigid and fibrous; the anterior and right posterior

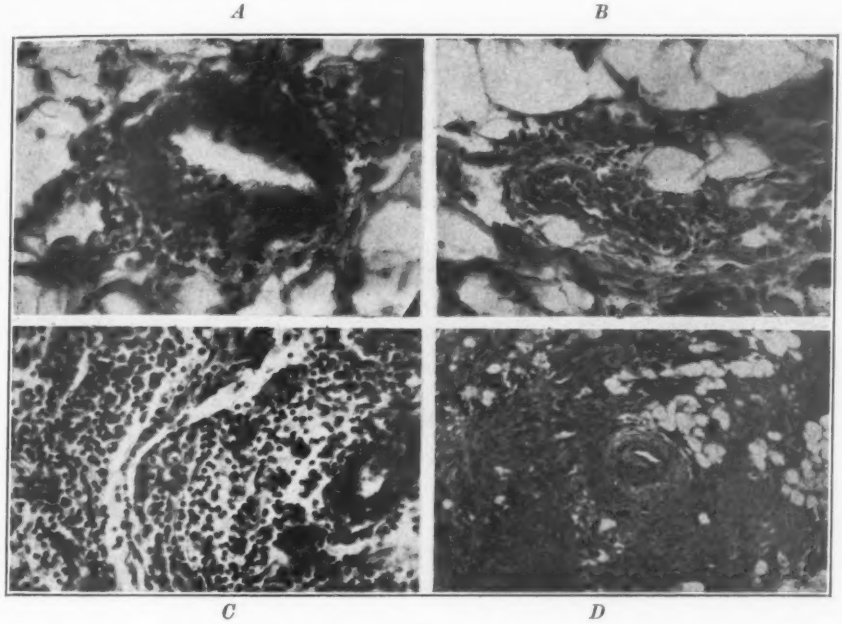

Fig. 5.—Photomicrographs of sections of the auricular wall near site of rupture. *A*, and *B*, perivascular lymphocytic infiltration; *C*, cellular infiltration containing many red blood cells; and *D*, branch of coronary artery in auricular wall showing almost complete occlusion.

cusps were firmly united by dense fibrous tissue forming a thick, reddish, elevated ridge on the upper surface of the valve. The mouths of the coronary arteries appeared small but were not occluded. The myocardium was normally thick and firm, and showed a few grayish streaks, most abundant in the interventricular septum. The coronaries appeared normal. There was no sclerosis or intimal thickening.

Microscopic sections showed evidence of disease of the coronary arteries. In the smaller branches within the ventricles there was distinct intimal thickening and fibrosis with great contraction of the lumina. The vessels of the epicardium in many instances contained completely hyalinized thrombi. There was no calcification. A few scattered patches of fibrosis were found in the myocardium and a slight general increase of intermuscular connective tissue. The epicardium contained many thick patches of fibrous tissue. In the aortic valve masses of old fibrous tissue,

largely calcified, were found. At the base of the valve distinct bone formation had occurred with osteoclasts, lacunae and a configuration simulating Haversian canal systems.

Sections of the right auricular wall near to and remote from the site of rupture showed thickening and extensive infiltration of red blood cells. A thin film of hyalinized material was present on the pericardial surface. The subpericardial tissue and muscle showed considerable disorganization due to edema and cellular infiltration. Many polymorphonuclear leucocytes were present, and these, together with other cellular elements, showed considerable karyorrhexis. Many of the small vessels showed intimal thickening, hyaline change and great contraction of the lumens. (Fig. 5.)

In the case here reported it appears that although the main coronary vessels were comparatively normal, the smaller branches were markedly altered. The prominent intimal thickening and the presence of hyaline material simulating thrombi suggest that the initial symptoms were due to infarction of the auricular wall and interstitial hemorrhage. These changes caused sufficient weakening of the wall to lead to rupture and hemopericardium.

There was no finding at autopsy to explain the difference in blood pressure noted between the right and left arms.

DISCUSSION

An analysis* of 55 cases of rupture of the auricle (54 from the literature plus the one here described), reveals certain interesting facts. Auricular rupture in contrast with ventricular, occurs more frequently at younger age periods. Thus, in 44 instances of ruptured auricle, 21 or 47.7 per cent were found in individuals under forty years. This incidence is seven times as great as that given for all ruptures of the heart, where only 6.7 per cent occur before the fortieth year.[5] Males are more often the victims of rupture of the auricle than are females, in the proportion of 30 to 16, in 46 cases where the age was recorded. The site of rupture was as follows in 55 cases: right auricle 39, left auricle 15, and interauricular septum 2 (one case had tears both in right auricle and in septum). Trauma, either trivial or severe, was found to be a primary cause in six instances. Exertion seems rarely, if ever, to have produced the rupture, the attack developing suddenly while the patient was in bed, walking, standing or engaged in his usual activities. Rowing a boat, straining at stool or vomiting are described as preceding the onset of an attack.

The clinical picture closely resembles that of coronary occlusion. In the majority of cases, 30 out of 46, death occurs almost immediately without premonitory symptoms—the patient giving a sharp cry or groan and falling unconscious. Less frequently a longer period elapses before death, varying from an hour to seven days, during which time symptoms of severe precordial, substernal or upper abdominal pain, nausea, vomiting, dyspnea, cyanosis, clammy cold skin, rapid weak pulse, signs of heart failure and falling blood pressure may develop. The presence of fever and electrocardiographic changes described in our case have not been recorded before in the literature.

*This analysis with full bibliography will be published elsewhere at a later date.

The pathological findings in the series of 55 cases are limited for the most part to brief descriptions of the gross appearance of the heart. Hemopericardium was present in the majority of instances, absent in a few, and not mentioned in the remainder. Escape of blood into the pleural cavity is described in a few cases where the pericardium was adherent, or where rupture occurred behind the pericardium. The tear averaged about ½ to ¾ inch in length as a rule, and the auricular wall is described as being unusually thin near the point of rupture. In the majority of reports no mention is made of the condition of the coronary arteries. In a few instances these are described as being sclerosed. There are only 9 cases in the series of 55 in which microscopic examination of the heart was made. Several of these note the presence of interstitial hemorrhage in the auricular wall, accompanied by intimal thickening of the smaller coronary artery branches, a process of obliterating endarteritis, leading to infarction of the auricular muscle.

The mechanism of rupture of the auricle, therefore, if one excludes the traumatic cases, would seem to be similar to that of rupture of the ventricle, and to be dependent upon disease of the nutrient arteries. In the former the vascular changes are largely confined to the smaller vessels in the atrial wall detectable only by microscopic examination, while in ventricular rupture changes such as extensive atheroma, narrowing or thrombosis of large coronary branches are generally visible to the naked eye. We believe that spontaneous rupture of the auricle does not occur in normal hearts if the traumatic cases be excepted, and that in the future careful histological studies, if made, will show a pre-existing obliterative endarteritis, such as has been described in the case reported above. The cause of death is not fully understood, although in the ruptures with extensive hemopericardium the increased pressure within the pericardial sac, especially if it develops quickly, is believed to produce anoxemia of the heart muscle, resulting in death. This theory has some experimental support, such as Cohnheim's tamponade investigation, but does not explain death in the instances where the pericardial cavity contains no blood.

SUMMARY

1. A case of apparently spontaneous rupture of the right auricle is reported in a supposedly normal individual where trauma and excessive exertion were absent.

2. Serial electrocardiograms in this case showing changes suggestive of coronary occlusion are presented for the first time.

3. Histological study revealed a pre-existing obliterating endarteritis with interstitial hemorrhage and infarction of the auricular wall, leading to rupture, a process essentially similar to that causing rupture of the ventricle.

4. The clinical and pathological features of rupture of the auricle based on a review of 54 cases in the literature, plus the one here described, are discussed.

5. The large incidence of rupture of the auricle before the fortieth year of life, 47.7 per cent, as against 6.7 per cent for ventricular rupture, is pointed out.

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CHANGES IN THE RS-T COMPONENT OF THE ELECTROCARDIOGRAM PRODUCED BY EXPERIMENTAL RUPTURE OF THE AURICLE OF THE DOG'S HEART AND BY PERICARDIAL INJECTION*

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INTRODUCTION

THIS study was prompted by the occurrence of spontaneous rupture of the auricle in a patient seen in consultation by one of us (L.W.G.) in April, 1930. A report of the case has been presented in the preceding article by Clowe, Kellert, and Gorham. The outstanding feature of it was the almost exact duplication in symptomatology of coronary occlusion, and this clinical diagnosis was apparently supported by changes in the electrocardiogram presumably characteristic of such an accident. The finding post mortem of coronary arteries normal in the gross, and of a patent tear in the right auricle, together with a marked hemopericardium, suggested that the electrocardiographic changes were not in this instance diagnostic of coronary disease, but were due either to the auricular damage or to the hemopericardium. In order to determine whether or not similar changes in the electrocardiogram could be produced by experimental rupture of the auricle, these experiments were undertaken.

REVIEW OF PREVIOUS EXPERIMENTAL WORK DEALING WITH THE PRODUCTION OF RS-T CHANGES IN THE ELECTROCARDIOGRAM

In the past few years numerous papers dealing with experimental alterations in the electrocardiogram have been published, with reviews and discussions of previous work. Our discussion will be limited to the RS-T component of the cardiogram, and the literature cited will serve as a guide to practically all of the publications, in this special field, of the past decade as well as to the earlier work.‡

The literature of experimental studies on the T-wave alone had already become very extensive by 1925, as the review by Katz[1] then showed. Thomas Lewis[2] was apparently the first to engage in work on coronary artery ligation, with electrocardiographic controls. However, F. M. Smith[3] seems to have priority in this field as far as special refer-

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‡Extended recent discussions of various aspects of the problem of alteration of the electrocardiogram consequent to myocardial changes due to various conditions acting directly or indirectly on the heart can be found in the papers by Damir and Lampert, Feil and associates, Crawford and coworkers, Barnes and Mann, Katz, and others, cited in this review.

ence to the coronary type of T-wave is concerned. Using dogs, he observed that coronary ligation resulted in a T-wave form very similar to that in a proved clinical case of coronary thrombosis, which case was later described by Herrick.[4] Smith extended his research in 1920.[5] Ligation experiments with electrocardiographic records were later made on dogs by Sutton and King,[6] Otto,[7, 8] Parade,[9] Averbuck and Rachmilewitz,[10] Feil, Katz, Moore and Scott,[11] Damir and Lampert[12] and by Barnes and Mann.[13] Gold, DeGraff and Edwards[14] used cats in similar experiments.

There is general agreement that coronary artery ligation in dogs produces changes in the RS-T component resembling, especially in the early stages of the process, those resulting from myocardial infarction in man; but all the factors involved are not fully understood. Parade observed that by the time the coronary type of T-wave has developed the damaged area has already begun to organize. Feil and associates found that after ligation an increasing anoxemia was necessary to insure, within an hour or so, the changes in the electrocardiogram, and they concluded that coronary obstruction was only one factor. On the other hand, Barnes and Mann did not emphasize the anoxemia element but pointed out that the RS-T changes are inconstant owing to peculiarities of the arterial distribution in the dog's heart which make it difficult, if not impossible, to reproduce the late electrocardiographic changes seen in myocardial infarction in man. Katz and Wallace[15] also showed the relation between clinical and experimental electrocardiograms and pointed out the errors which are likely to creep into such work. In their extensive study Damir and Lampert[12] found not only real differences between the cardiograms following cardiac infarction in man and the dog, but also features common to the two types. They likewise discussed at length the relations between the form of the electrocardiogram and infarction.

It may be mentioned at this point that in a number of cases of stab wounds of the human heart, with consequent damage or obstruction of coronary arteries, changes in the electrocardiogram have been observed which are very similar to those due to the ordinary thrombotic coronary occlusion in man and to coronary ligation in animals. Such cases have been reported by Davenport,[16] Puccinelli,[17] Cole,[18] Bates and Talley,[19] Schlomka,[20] Purks,[21] Elkin and Phillips,[22] and by Porter and Bigger.[23]

The researches of Otto,[24] Averbuck and Rachmilewitz,[10] McGuire[25] and Damir and Lampert[12] on the changes of the RS-T component caused by chemical injury of the myocardium, by cooling it, by coronary ligation, by stimulation of the cardiac sympathetic nerves and by excision of the stellate ganglia are important. Although there is some disagreement among the above mentioned and other investigators regarding the actual rôle and importance of different factors in the origin and subsequent changes in the RS-T component, the results furnish accumulat-

ing evidence that certain features, at least, of the coronary type of T-wave can be produced by a variety of means. An observation of much interest in this connection is one by Damir and Lampert[12] who found that in a number of dogs excision of the left stellate ganglion produced T-wave changes resembling certain of those produced by coronary ligation, although there was no myocardial damage. They also found that RS-T abnormalities caused by silver nitrate injury of the heart or by coronary ligation could sometimes be made to disappear by removal of the right stellate ganglion. These experiments, and some by Otto,[7] Averbuck and Rachmilewitz,[10] and McGuire,[25] on the extracardiac nerves, suggest an important nervous factor in the production of abnormalities of the RS-T component but leave some points obscure. Confirmation of certain of the experimental results reported is desirable.

In the past the lack of uniformity in the correlation of the RS-T changes and cardiac injury has been partly due to the technic employed. Recognizing the difficulties of confining a lesion to a definite part of the ventricles, Crawford and associates[26] employed the electric cautery, using the cat heart. They state that lesions in similar sites produced, with almost complete consistency, the same type of RS-T deviation. They are of the opinion that the geographical situation of the lesion, rather than the distribution of the blood supply, determines the character of the electrocardiographic changes. Nevertheless, other recent work has emphasized the importance of the arterial distribution in the heart (Otto,[8] Parade,[9] Barnes and Mann[13]).

Changes in intracardiac pressure (Otto,[27] Lian and Marklen[28]) alter the RS-T complex in a suggestive way, and injections of isotonic saline solution and of oil into the pericardial sac can, by pressure, produce RS-T changes similar to those in certain stages of clinical cases of coronary occlusion (Katz, Feil and Scott,[29] Scherf[30]). We have also confirmed this observation in our work, as will be noted later.

It is well known that drugs of various kinds can invert the T-wave, and not infrequently the RS-T deviations are similar to those under discussion. For this reason digitalis and other glucosides are of obvious importance. However, there is marked disagreement in the reports on these glucosidal effects in animals (Grünbaum[31],* DeGraff and Wible,[32] and Brams and Gaberman[33]). In a dozen or more experiments on cats and dogs RS-T changes somewhat similar to those of the coronary type have been seen in our laboratory. They were produced by ouabain and strophanthidin under certain conditions and will be described in a later paper.

Finally, we mention the recent work of Kountz and Gruber[34] and of Kountz and Hammouda[35] on anoxemia of the heart. The former workers found that when the oxygen content fell below 50 per cent of normal in

*The experiments of Grünbaum have to do only with changes in the electrocardiogram of man.

the arterial blood of dogs during rebreathing experiments the electrocardiogram showed changes strikingly similar to those of coronary occlusion in man. Gruber and Kountz[36] also showed that coronary arterial constriction produced by pitressin can provoke marked RS-T alterations. Kountz and Hammouda[35] have extended this work, using the heart-lung preparation, and have obtained evidence that metabolites, rather than anoxemia alone, acting locally on the myocardium are responsible for the RS-T effects, though the combined factors of deficient oxygen and excess carbon dioxide may also produce them.

It has become increasingly apparent, from both clinical and experimental work of the past ten years, that fusion of the T-wave with the RS segment of the electrocardiogram is not pathognomonic of coronary occlusion, though serial cardiograms in suspected cases furnish very suggestive evidence of such obstruction in many instances (Cooksey and Freund[37]). From the experimental work reviewed it is evident that, apart from direct myocardial damage or necrosis by any agency mentioned, many of the procedures used to affect the ventricular musculature indirectly have, as a common result, the production of myocardial ischemia of greater or lesser degree and extent. It seems reasonably clear that although in such cases anoxemia alone is not the sole factor in producing the RS-T changes it may bring them about when associated with an excess of metabolites, as the experiments of Kountz and Hammouda[35] indicate. Further correlation of the results of experimental study of the RS-T portion of the electrocardiogram is desirable.

DESCRIPTION OF EXPERIMENTS

A. Auricular Rupture

Dogs were chosen as the experimental animals. Three preliminary experiments were performed in which the chest was opened under morphine and ether anesthesia and the right auricle was cut or torn to produce bleeding into the pericardial cavity, the latter being closed by a purse string suture. Electrocardiograms taken before and after this operation showed no significant changes as a result of either the auricular injury or the hemopericardium. No attempt was made in these first three experiments to preserve aseptic technic or to keep the animals alive beyond a period of a few hours.

Following the preliminary experiments a more or less standardized technic was adopted which may be described as follows:

An electrocardiogram was taken by the three standard leads, before anesthetizing the animal. It was found convenient and entirely satisfactory to use electrodes consisting of three or four turns of No. 18 copper wire wrapped about the legs of the dog after first scrubbing the hair with strong salt solution and applying about a yard of heavy web bandage two inches wide soaked in the same solution. This is the procedure recommended by Herrmann and Wilson.[38]*

The dog was then given 40 to 50 mg. of sodium amytal per kilogram of body weight. This was given intraperitoneally and was supplemented by ether, if neces-

*The peaks of the R and S deflections, being almost invisible in most of the records, have been retouched with white ink in order to indicate the amplitude of those two waves.

sary, to produce surgical anesthesia. A second electrocardiogram was taken after anesthesia had been induced. The chest was then opened under aseptic precautions, the respiration being maintained by an air pump connected with a tracheal tube. The opening made in the chest wall was on the left side between the third and fourth or fourth and fifth ribs. A sketch showing the incision is seen in Fig. 1. The pericardium was picked up with a clamp, and a purse-string suture of fine fishline was placed about the tip of the clamp. Then through a small opening made in the pericardium inside the purse-string suture a clamp was passed back toward the base of the heart, and the right or left auricular appendage was grasped and drawn out through the opening in the pericardium. (The left auricle is easily seen through the pericardium and is much more accessible, but the right auricle was used in a majority of experiments in order to duplicate more exactly the condition present in the case of spontaneous rupture referred to above.) A curved clamp was then placed on the auricular appendage about three-eighths of an inch

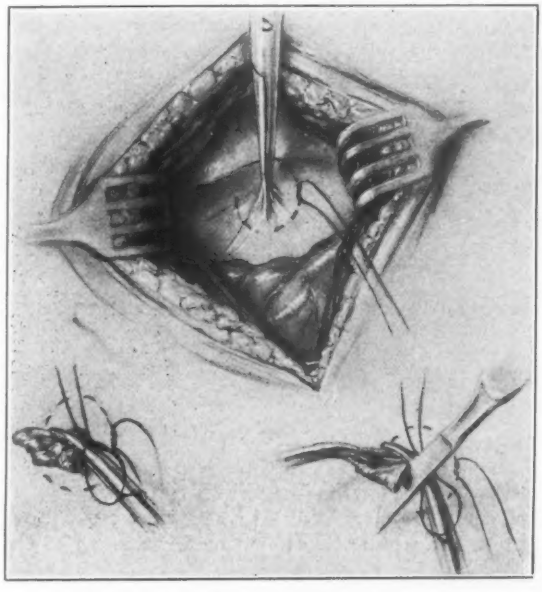

Fig. 1.—Upper: Drawing of operative field with clamp picking up pericardium and purse-string suture in place.
Lower left: Tip of auricular appendage in clamp with slip tie in place.
Lower right: Tip of auricular appendage being cut away.

from the tip. Back of the clamp was then tied a slip ligature of strong fishline drawn tight. A knot was tied in the slip end of the tie for identification and this was brought out through the chest wall. The other end was cut off close to the tie. A second fishline suture was placed through the wall of the auricle directly back of the tie and the two ends were brought outside. (The purpose of this so-called "saw string" will be described later. It was not used in all experiments but was found very important.) The tip of the auricular appendage was then cut off close to the clamp, the clamp removed carefully and the auricle allowed to slip back to its normal position within the pericardium. The purse string in the pericardium was drawn, closing the opening. The chest wall was closed by three layers of sutures, the artificial respiration was stopped, and another electrocardiogram was taken after the animal had resumed normal breathing. In one to three days after the operation, the string which controlled the slip tie on the cut auricle was

drawn out and the second ligature which had been placed in the wall of the auricle was torn out by sawing back and forth until it cut through the muscle. The use of the saw string was essential to insure free bleeding from the auricle. It had been found that the cut end of the auricular appendage was sealed by clot formation within twenty-four hours so that little or no bleeding would occur on removing the slip ligature unless the wound were freshly torn open. Electrocardiograms were taken before, during, immediately after this procedure, and at varying intervals over periods ranging from several days to two months.

Protocols of Typical Experiments.—

January 27, 1932. Experiment 18.

Dog 40, male, three and one-half months old, weight 12.6 kg. Electrocardiogram at 8:20 P.M. (3 leads), followed by sodium amytal (50 mg. per kg.), intraperitoneally. Well anesthetized at 8:50 P.M. when a second electrocardiogram was taken. Operated upon as described above, removing the tip of the right auricular appendage. No bleeding. Purse string drawn in pericardium; chest closed and bandaged. Very little ether was required. Dog appeared in good condition. Third electrocardiogram taken.

January 28. 9 A.M. Animal somewhat under the influence of amytal but tried to stand. Drank water.

January 28. 4 P.M. Dog able to walk. Electrocardiogram taken at 4:15 P.M. Bandage removed and incision opened at one end to locate buried strings. "Slip string" pulled at 4:35 P.M. followed immediately by the "saw string." Electrocardiogram taken at once and another after ten minutes. Animal in good condition.

January 29. Dog active and apparently normal. Electrocardiogram at 11:30 A.M.

Further electrocardiograms were taken as follows: January 30 and 31. February 1, 2, 3, 4, 6, 9, 15, 19, and 29.

Electrocardiographic Changes.—The electrocardiogram taken January 27 before operation is shown in Fig. 2. It is a perfectly normal tracing but the rate is fairly rapid. The records taken immediately following the operation show no change of any consequence. The first marked variation appears in the tracing taken January 29 at 11:30 A.M., nineteen hours after pulling the string to produce hemorrhage into the pericardium. This record is shown in Fig. 3. Here is found sharp inversion of T-waves in Leads I and II with decided elevation of the S-T interval. The T-waves take off 1-2 mm. above the base line, and the S-T line is definitely convex upward. The next day the T-waves are upright in all leads, but the take-off remains high. Fig. 4 shows the record obtained February 6, nine days after pulling the string. Here we find very high T-waves, especially in Lead II, and a high take-off in all leads. From this time on repeated tracings showed a gradual return to normal. On February 29 the last record was taken. This is reproduced in Fig. 5, and except for a slight elevation of the S-T interval, it is seen to be practically the same as the original tracing taken before operation. Consequently this dog was used again for a second experiment which is next described.

February 29, 1932. Experiment 23.

Dog 40, male, four and one-half months old, weight 15.3 kg. This dog was first operated upon January 27, the tip of the right auricle being cut away at that time. The second operation was exactly the same as the first except that the tip of the left auricle was removed. Electrocardiograms taken. Animal in good condition.

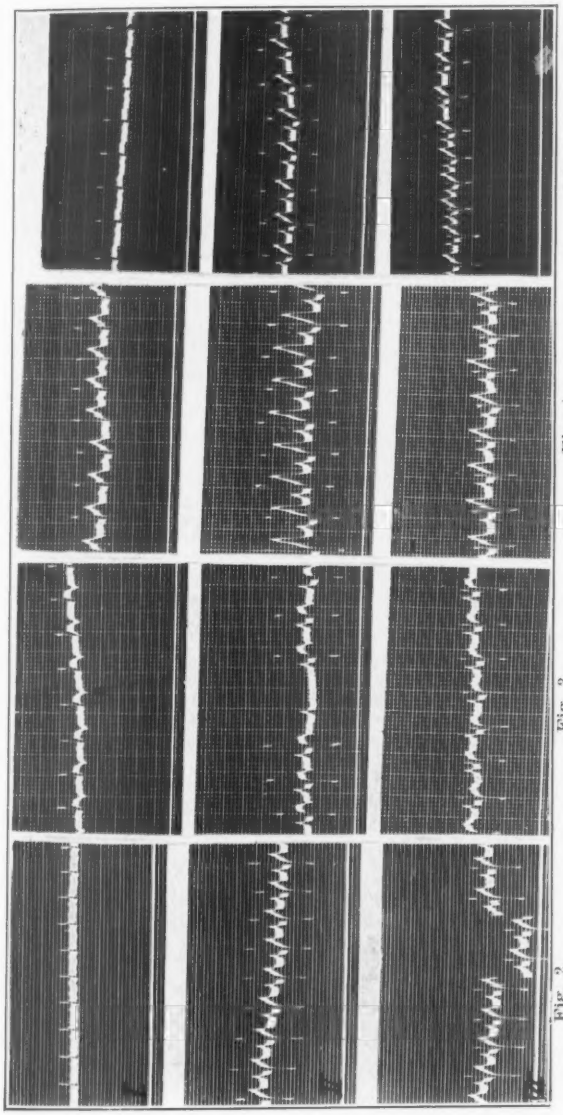

Fig. 2. Fig. 3. Fig. 4. Fig. 5.

Fig. 2.—Experiment 18, Dog 40. Before operation.
Fig. 3.—Nineteen hours after pulling string. Note inversion and high take-off of T_1 and T_2. A-V block in Lead II.
Fig. 4.—Nine days after pulling string. Note high T-waves with high take-off.
Fig. 5.—Thirty-two days pulling string. Note return to near normal. This serves as control for Exp. 23 in which dog was again operated upon.

March 1. 9 A.M., Dog lying on side still under effect of amytal. 1 P.M., Animal able to walk about. 1:15 P.M., Electrocardiogram. 2:05 P.M., Slip string pulled, followed by "saw string." Electrocardiogram taken during and after pulling string. 5 P.M., Electrocardiogram.

March 2. 9 A.M., Dog up and about but not active. Some infection around

sutures. 10:30 A.M., Electrocardiogram. This showed a return of the characteristic changes in the form and take-off of the T-waves in all leads. Therefore, at 2:30 P.M. the same day, the dog was again anesthetized and the heart exposed through the original incision to determine the amount of blood in the pericardium. The latter was found greatly distended with fluid. By means of a syringe and needle 90 c.c. of dark red bloody fluid were removed from the pericardial sac besides about 20 c.c. which were lost by leakage around the needle. Chest again closed and an electrocardiogram taken. Dog in fair condition.

March 3. 9 A.M., Dog moved about, but was not active. 10:45 A.M., Electrocardiogram. Repeated at 3:20 P.M. The dog was then sacrificed and an autopsy done. The left lung was found adherent to the chest wall and to the pericardium. The latter was thickened, injected and very friable. Bloody fluid oozed from the opening made by the needle used the day before for aspiration. The pleural cavity contained 72 c.c. of bloody fluid, part of which had leaked from the pericardium. The pericardial sac contained 42 c.c. of similar material. No adhesions between pericardium and heart wall. Right auricular appendage missing and wound fully healed. Left auricular appendage also missing and wound closed by mass of fibrin. Opening not patent but on pressure blood was forced out from left auricle.

Electrocardiographic Changes.—Three hours after pulling the string, the characteristic changes in the form and take-off of the T-wave begin to appear in Lead I. The electrocardiographic record before operation is seen in Fig. 5, and the record taken three hours after producing hemorrhage into the pericardium is shown in Fig. 6. Twenty hours after producing a hemopericardium the changes are more pronounced as shown in Fig. 7. Here the T-waves are inverted in all leads, and the take-off is elevated in Leads I and II. Four hours later the T-wave in Lead III is found upright, but otherwise the picture is essentially the same (Fig. 8). Following the removal of bloody fluid from the pericardium by aspiration T_3 becomes inverted again, and now in all leads we find inverted T-waves and a high take-off (Fig. 9). Nineteen hours after removing the blood from the pericardial sac, the changes are even more pronounced (Fig. 10). The T-waves are still inverted in all leads, and the take-off is higher than before.

The interesting point in this experiment is the fact that it was the second time that such electrocardiographic changes had been produced in the same dog by a second auricular rupture and a consequent hemopericardium. Of further interest is the fact that these changes not only persisted but were intensified after removal of a large part of the blood from the pericardium. It would appear that these changes were evidence of a myocardial disturbance which persisted after release of pressure within the pericardial sac.

Review of Auricular Rupture Experiments.—The series comprised in all, 18 experiments on 16 dogs. The right auricle was opened in eleven instances, the left in seven. Definite electrocardiographic changes were obtained in eight experiments, or 44.4 per cent. The right auricle was opened in five of these and the left in three. However, in only eleven of the eighteen experiments did the dogs survive the operation for twelve hours or longer. In other words, there were only eleven instances in

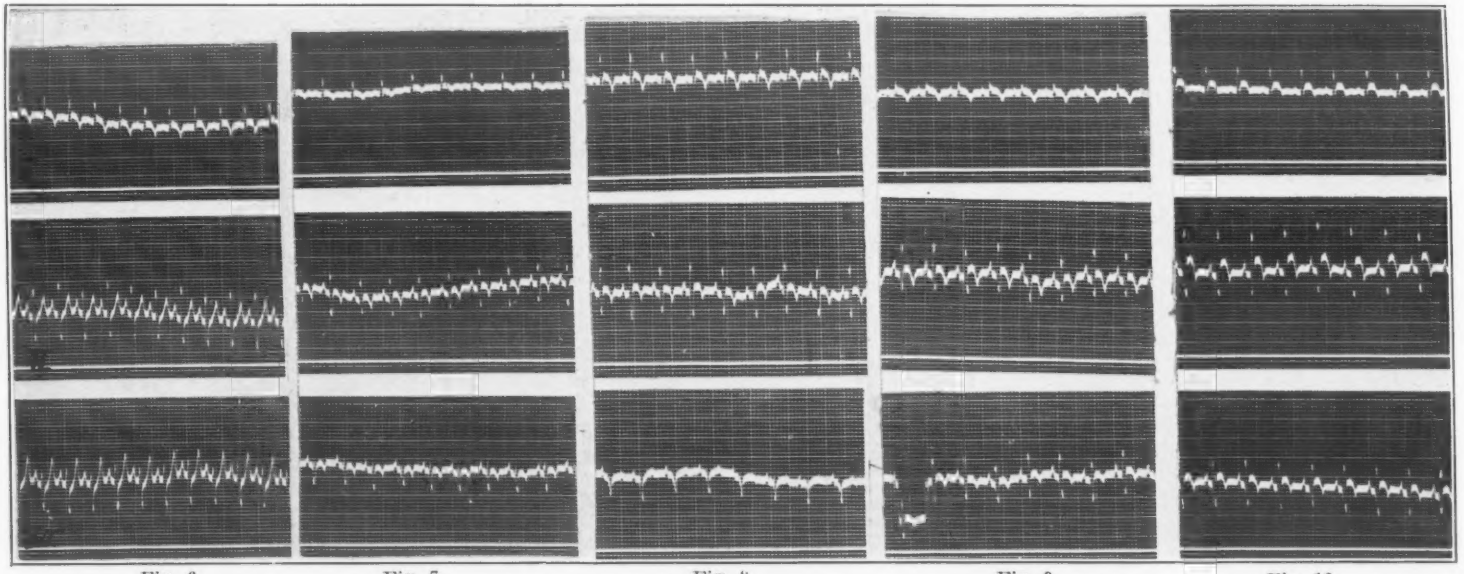

Fig. 6. Fig. 7. Fig. 8. Fig. 9. Fig. 10.

Fig. 6.—Experiment 23, Dog 40. Three hours after pulling string. Note inversion and high take-off of T_1. Compare Fig. 5.
Fig. 7.—Twenty hours after pulling string. All T-waves now inverted with ST interval elevated and convex upward.
Fig. 8.—Twenty-four hours after pulling string and just before removing blood from pericardium. T_3 upright.
Fig. 9.—Immediately after removing 90 c.c. of blood from pericardium. T_3 again inverted. High take-off in all leads.
Fig. 10.—Nineteen hours after removing 90 c.c. of blood from pericardium. Note extremely high take-off and persistent inversion of T-wave.

which the animals lived a sufficient time for electrocardiographic changes to develop. Of this number eight showed the alterations that have been described above, a percentage of 72.7. In three cases no changes could be detected. Of this number two experiments were on the same dog. No "saw string" was used in either to insure opening the auricular wound, and it is probable that no appreciable hemorrhage into the pericardium occurred. Autopsy three days following the second experiment on this animal showed no evidence of bleeding from the auricle into the pericardium. The other failure was in the first experiment of this series. In this case the electrocardiograms were not taken at the right time and only one lead was used.

In seven dogs death occurred within twelve hours after operation. The causes of death in these cases were determined as follows:

Failure of slip ligature to hold, four; prolonged operation and anoxemia, one; pulmonary embolism, one; slip string pulled too soon (fifteen minutes) after closing chest, one.

Survival Period.—Of the eleven experiments in which the dogs lived more than twelve hours, the survival period was from three to sixty-four days. All animals were sacrificed eventually except one which developed a severe wound infection with a pyopneumothorax resulting in death on the sixth day after operation.

Use of "Saw String."—The importance of the "saw string" to insure bleeding cannot be overemphasized. The healing process was apparently so rapid and the intra-auricular pressure so low that there was little likelihood of bleeding from the cut auricle unless the wound was re-opened. Simply untying the ligature was not enough to tear apart the edges of the cut auricle after healing had gone on for twenty-four hours or longer. This was accomplished readily by the use of the "saw string." In no case where this means was used to insure bleeding, and in which the dog survived the operation, did electrocardiographic changes fail to develop.

Blood Pressure in the Brachial Arteries.—Since one of the striking features of the clinical case of spontaneous auricular rupture previously mentioned was the difference in blood pressure in the two arms, this point was investigated in the experimental series. Blood pressure in both brachial arteries was recorded by means of a mercury manometer in three animals with experimental auricular rupture showing definite electrocardiographic changes. The pressure was found to be the same on the two sides in every case and within normal limits.

B. Pericardial Injection

In this series of experiments it was decided to introduce blood and other fluids into the pericardial cavity by means of a needle, thus eliminating direct mechanical injury to the auricular wall. The technic of this operation was as follows:

An electrocardiogram was taken and the dog was anesthetized with sodium amytal and ether. The chest was opened in the same way as previously described. The pericardium was picked up at a point on the left side about midway between the base and the apex. A very small needle hole was made, just large enough to allow the edges to be grasped by two mosquito clamps. A short blunt hypodermic needle, No. 20, was introduced through the opening and the edges were drawn out along the needle by means of the small clamps. Then a strong fishline tie was placed about the conical projection of the pericardium along the needle, and this ligature was drawn tight about the needle. The fluid, warmed to 39° C., was then introduced by means of gravity or a large syringe until the desired amount had been used. The tie was then drawn tight on the needle by one operator while another slowly withdrew the needle from the pericardium. In this way the opening was tied off completely without leaving needle holes from which the fluid might leak. The chest was then closed, an electrocardiogram was taken at once, and repeated once or twice daily during survival of the animal. A typical experiment of this series is described below.

Protocol of Typical Experiment.—

January 11, 1932. Experiment 15.

Dog 37, female, weight 12.8 kg. An electrocardiogram was taken and the dog anesthetized with sodium amytal (50 mg. per kg.) intraperitoneally. After another electrocardiogram, the chest was opened and a No. 20 blunt hypodermic needle was tied into the pericardium as described above. Seventy cubic centimeters of blood serum obtained from another dog were then slowly introduced. This produced a weak heart beat, and it was feared that more pressure would kill the animal. The pericardium was tied off as the needle was withdrawn and no leak developed. Chest was closed and the dog began breathing. Another electrocardiogram was taken, and the animal was placed in cage still under deep anesthesia. Condition did not appear to be good.

January 12. 9 A.M., Dog lay flat on side, still under effect of amytal. Breathing somewhat labored. 10:30 A.M., Electrocardiogram. 5:30 P.M., Animal still lay flat on side. Drank water when aroused. Not able to stand.

January 13. 9 A.M., Animal stood up but did not move about. Drank water but refused food. 10 A.M., Electrocardiogram. 8:45 P.M., Electrocardiogram. Condition less favorable.

January 14. 9 A.M. Dog died. At autopsy many adhesions found in left pleural cavity with some bloody fluid and small amount of pus. Left lung partly collapsed and adherent to chest wall and pericardium, which was thick and injected. Opening made at operation was fully closed and no evidence of leakage of injected fluid. About 20 c.c. of bloody fluid found in pericardial sac. Surface of heart smooth and no adhesions between heart wall and pericardium.

Electrocardiographic Changes.—The first electrocardiogram taken after the injection of fluid showed very little change. The amplitude of the QRS had decreased, and there was a slight notching of the T-wave in Lead II and Lead III. Otherwise the picture was essentially the same as before operation. This was also true of the record taken thirteen hours after injection of the fluid. However, in thirty-seven hours a definite alteration was seen. T-waves were inverted in all leads, and the S-T interval was elevated and markedly convex upward (Fig. 11).

Review of Injection Experiments.—There were six experiments in this series, three of which were successful in that the animals survived for

more than twelve hours after operation. In all three electrocardiographic changes similar to those described were noted. The animals that died soon after operation showed no significant alteration in the electrocardiogram within the short time that elapsed before death.

The fluids used for injection were dog serum, olive oil, normal saline, and dog's blood kept fluid by the addition of heparin. The amounts used varied from 60 to 128 c.c., the largest volume employed without producing the animal's death being 90 c.c. Significant electrocardiograms were obtained in one animal after the injection of only 60 c.c.

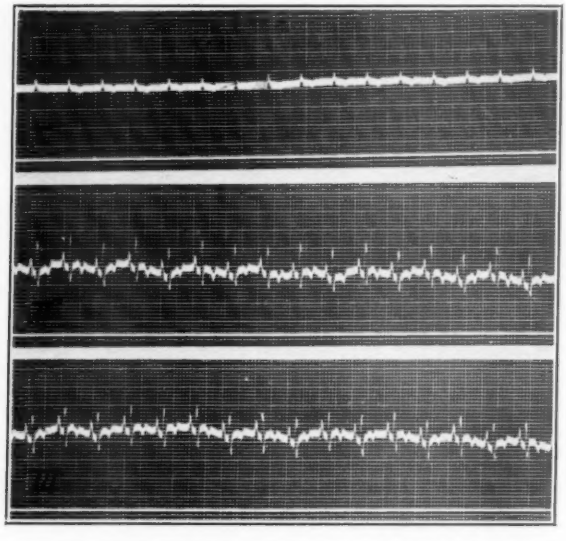

Fig. 11.—Exp. 15, Dog 37. Thirty-seven hours after injection of 70 c.c. of dog serum into pericardial sac. Note abnormal T-waves in all leads.

SUMMARY AND CONCLUSIONS

1. Experiments have been here described for the first time showing that alterations in the RS-T component of the electrocardiogram simulating those associated with coronary occlusion may be produced by experimental auricular rupture with resulting hemopericardium.

2. These electrocardiographic changes have not been found immediately after producing a hemopericardium but only following a time interval of several hours.

3. The changes have been observed to persist for some time after the absorption or withdrawal of the fluid from the pericardial sac.

4. The variations in the RS-T component were not due to the auricular injury but were associated with considerable amounts of fluid in the pericardial cavity.

5. The complete explanation of the mechanism of the production of the electrocardiographic changes in our experiments cannot be given, although the development of anoxemia as previously discussed may well be a most important factor.

6. Another method of producing RS-T changes in the electrocardiogram has been reported which adds to the existing evidence that the so-called coronary T-wave is not pathognomonic of coronary occlusion.

We desire to express our thanks to Miss Dorothy E. Chatfield, of the Albany Hospital, for assistance in the technical part of the experiments.

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THE RELATION OF THE INTRAPLEURAL PRESSURE TO THE MECHANICS OF THE CIRCULATION*

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IN A PRECEDING report of experimental studies we showed that there was an abnormally negative intrapleural pressure associated with experimental pneumonia, or with obstruction of the trachea or bronchi.

We observed at this time that obstruction of the trachea from within or without produced important effects on the filling and function of the heart, i.e., dilatation, cyanosis, anoxemia of the tissues, and changes in blood pressure and heart rate. It was further noted that injection of suitable intrapleural fluid exerted a definite beneficial action on both the pulmonic and general circulation in experimental pneumonia or conditions associated with partial obstruction of the trachea or bronchi.

In this paper we wish to report additional observations on the effects produced on the heart and circulation by variations of negative intrapleural pressure. It was our purpose to determine, if possible, the mechanical effects produced by alterations of the intrapleural pressure both in the systemic or general circulation, and in the pulmonic or lesser circulation. The augmented negative pressure changes were produced by descreasing the inspiratory volume. This was accomplished by increasing degrees of tracheal obstruction. The diminished intrapleural pressure effects were produced by increasing the size of the tracheal opening. The respiratory volume was controlled by means of a specially devised tracheal tube (Fig. 1).

The mechanism by means of which the normal alterations in intrapleural pressure are produced is relatively simple when the anatomy and physiology of respiration are carefully analyzed. The relation of the heart to the lungs, and the lungs to the intrapleural spaces, from a study of cross- and sagittal sections can be readily appreciated (Fig. 2). It is obvious that changes of pressure in the intrapleural spaces must of necessity affect the filling and function of the heart. If the intrapleural pressure be rendered more negative, the inflow of blood into the right heart will be greater in a given period of time, i.e., during inspiration. It is chiefly this reduced pressure effect upon the heart and great veins which enables blood to flow upward from the more dependent portions, particularly the lower extremities, against gravity. To be sure, blood from the superior vena cava in the upright position will

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flow readily downward in its return to the right heart due to gravity, but in the prone position there will be relatively little difference from a theoretical point of view between the blood flow in the superior and inferior vena cava, as in this latter instance gravity affects both, approximately equally.

It is our belief that the rate of blood flow through the pulmonary circuit is largely determined by the intrapleural and intra-alveolar pres-

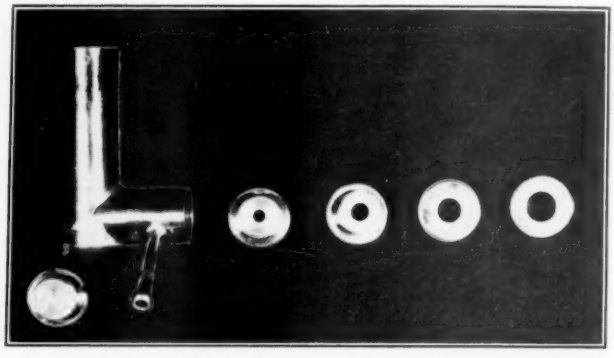

Fig. 1.—Tracheal cannula. Different sized stops may be screwed in the top of the cannula to control the volume of air entering or leaving the lungs. By means of the side arm, it is possible to measure the pressure within the trachea and bronchi by connecting it with a recording manometer.

Fig. 2.—Transverse section of thorax. Note pleural reflections in relation to the heart. Since each intrapleural space is a closed cavity, a reduction in pressure in any portion of the space will affect all parts approximately equally. It can be readily seen that a reduction in pressure in the intrapleural spaces will tend to increase the volume or dilate the heart.

sures. When the intrapleural and intra-alveolar pressures are greatly reduced, the rate of flow is diminished, and when these are less negative than normal the rapidity of flow through the pulmonary circuit is increased. The normal average rate of flow through the lungs depends upon a proper balance between the negative intrapleural and reduced intra-alveolar pressures. The mechanism for this, we believe to be as

follows: As the chest wall is lifted by muscle action, the two sides of the diaphragm descend synchronously. This constitutes a normal inspiration. At the very beginning of inspiration the chest wall and diaphragm begin to move away from the lungs. As the weight of the lung rests largely upon the diaphragm, the separation will probably not be as great between the lung and diaphragm as between the lung and chest wall in the upright position. As soon as the reduction in pressure created by the increased size of the intrapleural spaces becomes equal

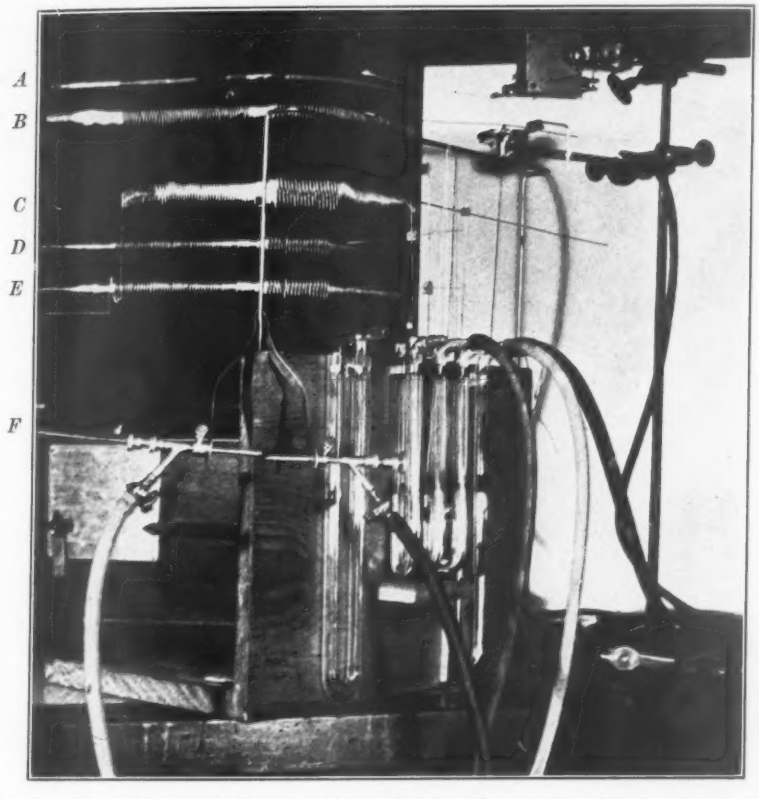

Fig. 3.—Apparatus used for recording intrapleural pressure, blood pressure, and excursions of the chest wall. *A*, time intervals; *B*, excursions of the chest wall; *C*, blood pressure tracing; *D* and *E*, intrapleural pressures; F, shows intrapleural needles and mechanism for holding them in place at any given distance within the intrapleural spaces. The U-tubes contain mercury with recording floats. Note the increased pulse pressure with increased negative intrapleural pressure.

to, or greater than, the elasticity and weight of the lung, the lung suddenly moves downward and outward to follow the movement of the chest wall and diaphragm. Due to the relatively small size of the tracheal opening (epiglottis) and the openings of the nose and throat (nasopharynx) a reduced pressure is developed during inspiration within the trachea, bronchi, and the alveoli. This reduction in pressure insures an adequate volume flow of blood to the lungs during inspiration. In ex-

piration the weight of the chest wall and the upward thrust of the diaphragm create a positive pressure within the alveoli, bronchi, trachea, and upper air passages, although the intrapleural pressure may still remain somewhat negative. This later observation can be explained only by assuming that the lungs do not completely fill the intrapleural spaces even during expiration (due to stretching of elastic tissue fibers within the lung). Furthermore, it must be assumed that gases are continually being absorbed from these spaces, thus keeping the pressure always subatmospheric. A positive pressure is essential within the lungs during expiration to facilitate removal of the accumulative waste products within the alveoli, particularly carbon dioxide, and also to insure proper

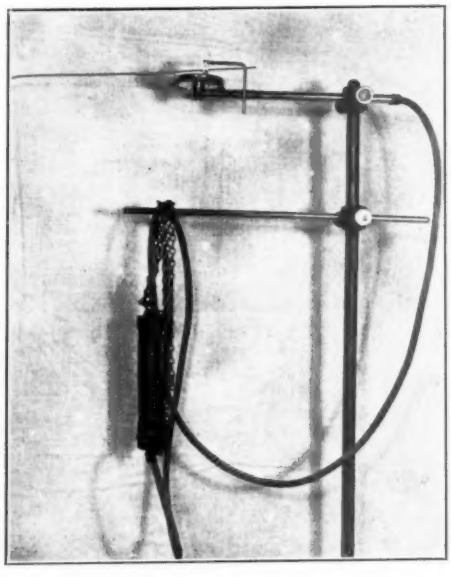

Fig. 4.—Apparatus for recording excursions of the chest wall. With inspiration the spring is elongated producing a reduction of air pressure in the closed system. These changes are transmitted to a recording tambour by means of a rubber tube connected to the side arm of the apparatus.

filling of the left auricle with oxygenated blood by compression and squeezing action. That these changes in pressure within the intrapleural spaces and lungs are of great physiological importance we have been able to demonstrate in the experimental animal.

THE EXPERIMENTAL METHOD

Healthy adult dogs were used as subjects for the experiments. Ether was chosen as an anesthetic, and a constant depth of anesthesia was maintained by the use of a standard gas-oxygen-ether machine. Bilateral intrapleural pressures were recorded on a smoked drug by connecting the needles within the pleural cavity to mercury columns (Fig. 3).

The excursions of the chest wall were recorded by means of a rubber covered spring and tambour (Fig. 4). The carotid artery was isolated, and a cannula was inserted which had been previously filled with a saturated sodium citrate solution, and this in turn was connected with the recording mercury column. The trachea was opened and the modified tracheal-cannula inserted. The trachea was then tied tightly about this so that all air entering or leaving the lungs passed through the cannular opening. By means of openings of various sizes it was possible to control the volume of air passing in and out of the lungs with each respiration. X-ray plates were taken in a number of the experiments without changing the position of the animal or the x-ray tube. In this way it was possible to record graphically alterations in the size of the heart that occurred during the experimental procedures.

We had previously noted variations of the venous pressure in our early experimental work. Many times the ordinary methods for visualization proved unreliable. A new type of venous pressure recording apparatus was devised to record graphically the rise and fall of pressure in the veins (Fig. 5). This consisted of

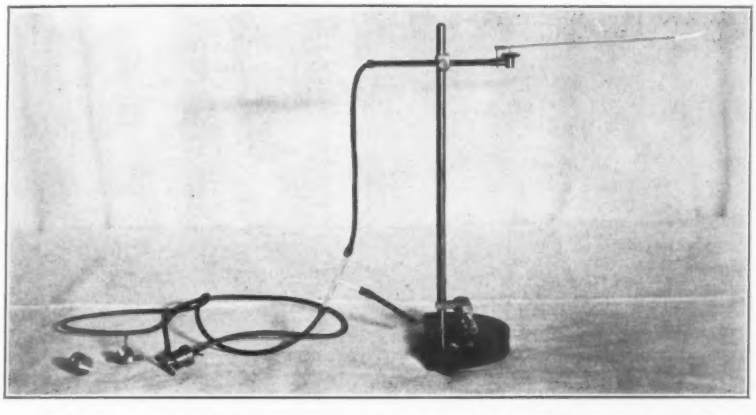

Fig. 5.—Venous recording apparatus. A thin rubber diaphragm is tied securely over the bowl. The upper portion is then screwed in place. The rubber tube and upper portion of the bowl is filled with Ringer's solution. The pressure changes are transmitted to the recording arm of the tambour.

a T-tube with a superimposed bowl which when correctly inserted lies parallel to the vein. The effects of gravity are thus largely eliminated. The tube is approximately the same caliber as the vein into which it is to be inserted. The bowl unscrews in the center and is covered by a rubber diaphragm. The surface of this is greased, and the upper portion of the bowl is screwed in place, filled with Ringer's solution, and connected to a recording diaphragm at approximately the same level as the femoral vein. A thin coat of paraffin is applied to the lower portion of the apparatus, i.e., that which comes in actual contact with the blood. This is necessary to prevent too early clotting. Any increase of pressure will thus produce bulging of the diaphragm and the pressure change will be transmitted to the fluid column of the recording diaphragm. When the pressure is reduced in the vein, blood flows out of the bowl, and the diaphragm becomes concave. The fluid column thus falls correspondingly and the change is recorded graphically on the smoked drum. The only difficulty we have encountered with this type of venous pressure recording apparatus is clotting of the blood, resulting from the slow flow produced in some of the experiments. There is a small sidearm to the instru-

ment through which Ringer's solution or saline can be injected to wash out clotted blood. In most instances this obviated the necessity of removing the apparatus from the vein.

The time intervals during the experiment were recorded by means of the usual clock mechanism and are marked on the drum at intervals of every five seconds. The heart rate was recorded in two different ways. Each systolic pulsation was recorded on the blood pressure tracing, and when the speed of the drum was increased it was possible to determine the rate, knowing the elapsed interval of time. The pulse rate was also recorded at ten- to fifteen-minute intervals by direct palpation of the femoral pulse. The rectal temperature was also taken at corresponding intervals and marked on the drum at the appropriate point.

Two general series of experiments were undertaken, first, a series with an abnormally increased negative pressure; and second, a series with a diminished negative pressure. In most instances, however, both experiments were performed on the same animal except where the experiment was allowed to go on to fatal termination. In some cases fluid was injected into the intrapleural spaces before beginning the experiment. The pressure was frequently recorded within the trachea in addition to the intrapleural pressure. The protocol of two typical experiments will serve to illustrate the method used.

PROTOCOLS

Dog 1.—An adult mongrel Police dog weighing twenty-one kilograms. Estimated age two years. Excellent general condition. Ether anesthesia. Intrapleural measurements, chest excursions, blood pressure, venous pressure, and intratracheal pressure were recorded on a smoked drum as previously described.

During the excitatory phase the negative intrapleural pressure was greatly increased, i.e., rendered more negative. As the stage of surgical anesthesia was reached, the intrapleural pressure became much less negative. With deep anesthesia it was correspondingly diminished. The blood pressure fell, venous pressure rose, and the pulse rate increased. Then the stage of poisoning was reached, and respirations ceased for two minutes. During the first ten seconds of this period the blood pressure fell fifteen millimeters and the venous pressure rose. The fall of blood pressure was followed in about one and one-half to two minutes by a rise of thirty-two millimeters. The blood pressure then gradually returned to the original normal level shortly after spontaneous respirations were resumed (Fig. 6).

A one-eighth inch stop was immediately inserted into the tracheal cannula, and the negative intrapleural pressure was at once increased to minus fifteen millimeters. Blood pressure was elevated, venous pressure at first fell, then rose slightly (Fig. 6), respirations slowed, and the heart became slow and irregular. In four minutes respirations ceased. Blood pressure promptly fell, although the heart continued to contract feebly. Venous pressure rose, then fell as the heart stopped two minutes later.

Post-mortem Findings.—Autopsy showed marked dilatation of the heart and great veins within the thorax as well as congestion of all the large veins within the abdomen. There was considerable congestion within the mesenteric vessels, with marked cyanosis, and in some instances areas of gross hemorrhage were visible. The lungs showed cyanosis and marked congestion, and the cut surface exuded dark red blood. There was some edema present but no definite pneumonia. This congestion was most marked in the bases but was also present throughout the

lungs. The liver bled freely when sectioned as did also the kidney. The venous pressure was apparently high in the vena cava. All of the superficial vessels were congested and this was particularly noted in opening the thorax.

Dog 2.—An adult mongrel dog weighing fifteen kilograms. Good general condition. Estimated age two to three years. Ether anesthesia. Intrapleural pressure, intratracheal pressure, blood pressure, venous pressure, and excursions of the chest

Fig. 6.—*A*, *B*, *D*, *E*, and *F*, are the same as in Fig. 7. *C*, intratracheal pressure tracing. This record shows exceedingly well the variations of the intrapleural pressure with anesthesia. Note on the left hand side of the record at second arrow the dog was light. Here the intrapleural pressure is tremendously increased, while excursions of the chest wall are diminished. A negative pressure also exists within the trachea, but is not as great as that in the intrapleural spaces. The third arrow marks the point just preceding acapnia, and here the dog was under relatively deep anesthesia.
The variations of blood pressure due to inspiration entirely disappear but promptly return with the resumption of active respiration.
Apnea was produced by overoxygenation. Note rapid fall of blood pressure and decreased pulse pressure. Asphyxial rise, then gradual return to normal with resumption of respiration.

wall recorded as in previous experiments. Pulse rate at beginning of experiment 120. Trachea opened widely. Intrapleural pressure promptly fell to minus one to two millimeters. Blood pressure decreased. Pulse rate increased to 160. Venous pressure rose. Body temperature fifteen minutes later had dropped to 100° F., and at the end of one-half hour to 97.8° F. Color as seen in tongue was pink.

Insertion of one-eighth inch stop produced prompt increase of negative intra-

pleural pressure, rise of blood pressure, and fall of venous pressure with slowing of heart rate and respiration. In twenty minutes the body temperature was 100.8° F., and there was moderate cyanosis. Removal of the stop resulted in first a rise, and then a fall of blood pressure. Usual changes in venous pressure occurred, i.e., rise of venous pressure as blood pressure fell (Figs. 7 and 8.)

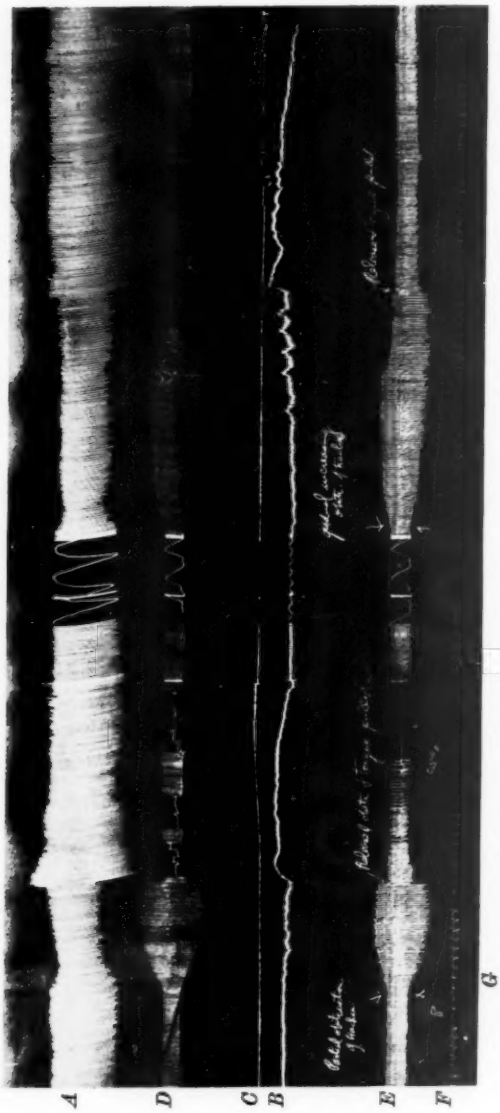

Fig. 7.—*A* represents excursions of chest wall; *B*, blood pressure tracing; *C*, the venous pressure changes; *D* and *E*, intrapleural pressure; *F* marks the time in five-second intervals. At *G*, the size of the air intake was reduced. Note the increased negative pressure which promptly occurred. When the intrapleural pressure was rendered less negative, note the fall in blood pressure and rise of venous pressure.

This experiment shows particularly well the diminished chest excursion which occurs with obstruction and increased intrapleural pressure.

Dog given oxygen and CO_2 under slightly increased pressure, i.e., greater than atmospheric. This produced a prompt rise of venous pressure and fall of blood pressure. *X*-rays taken in both inspiration and expiration showed the heart to be much smaller than normal (Fig. 10). In this animal *x*-ray plates were also taken

at the beginning of the experiment. In corresponding phases of respiration, the positive pressure was gradually increased and after twenty minutes the dog died.

Autopsy.—Temperature at time of death was 96.7° F. The skin was cold, there

Fig. 8.—*A*, *B*, *C*, *D*, *E*, and *F*, are the same as in Fig. 7.

Note the rapid rise of blood pressure with obstruction. The fall of blood pressure with inspiration and rise with expiration are well shown, as is also the increased pulse pressure present. The individual heartbeats may be seen in the more rapid portions of the drum tracing.

Note the additional rise of blood pressure after release of the obstruction, followed by rapid fall. This we believe is due to two factors: first, the increased efficiency of ventricular contraction as the intrapleural pressure becomes less negative; and second, the increased volume of blood delivered to the ventricle as the pulmonary stasis is relieved. This is well shown by the increased chest excursions.

was practically no bleeding in cutting through the thoracic muscles preparatory to opening the thorax. The lungs were pink and relatively avascular. Heart was small and contained very little blood. On opening the abdomen there was marked dilatation of all the mesenteric vessels. Pressure in the vena cava was exceedingly high;

liver was dark red in color and when sectioned a large amount of venous blood escaped. Kidney also showed the same congestion; spleen was contracted and firm. There was no free fluid in the abdominal cavity.

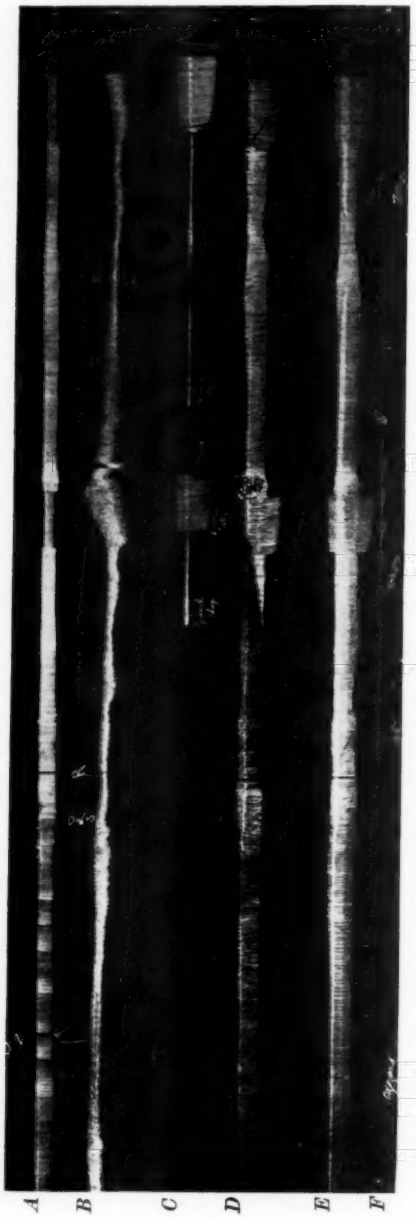

Fig. 9.—*A* represents excursions of chest wall; *B*, blood pressure tracing; *C* represents intratracheal pressure; *D* and *E* represent intrapleural pressure; *F*, time intervals.

At *G*, note where a 1/8" stop was inserted into the negative tracheal cannula, the marked increase in intrapleural and intratracheal pressures. The excursions of the chest wall were definitely diminished, the blood pressure became elevated, and the pulse pressure markedly increased. Also note the fall of intrapleural pressures with insertion of the 1/4" stop, and the gradual fall of blood pressure and diminished pulse pressure.

The increased width of the blood pressure tracing is produced chiefly by the fall of blood pressure with inspiration. Part of this is due to actual increased filling of the heart and in some instances actual insufficiency of the aortic valve occurs. The increased CO_2 also causes relaxation of the thin-walled veins. These changes will be discussed in more detail in relation to the chemical changes in the blood.

DISCUSSION

From the consideration of the data obtained from a large number of experiments, carried out on more than 40 dogs, a definite relationship appears to exist between the intrapleural pressure and the circulation.

When there is obstruction to the inlet of air, a reduction of intrapleural pressure invariably occurs. If of a sufficient degree, a reduction of pressure also occurs within the trachea, bronchi, and alveoli. Conversely, when the size of the tracheal opening is increased, the intrapleural pressure becomes less negative, and the intratracheal pressure is so near that of the atmospheric air that it cannot be recorded by means of a mercury manometer (Fig. 9).

These changes of intrapleural pressure promptly produce alterations in the pulmonary and general circulation, causing changes in the blood pressure, venous pressure, heart rate, and body temperature. The exact mechanism by which these changes are produced cannot be entirely explained on a mechanical basis alone, as the changes of pressure within the thorax, particularly those affecting the pulmonary circulation, not

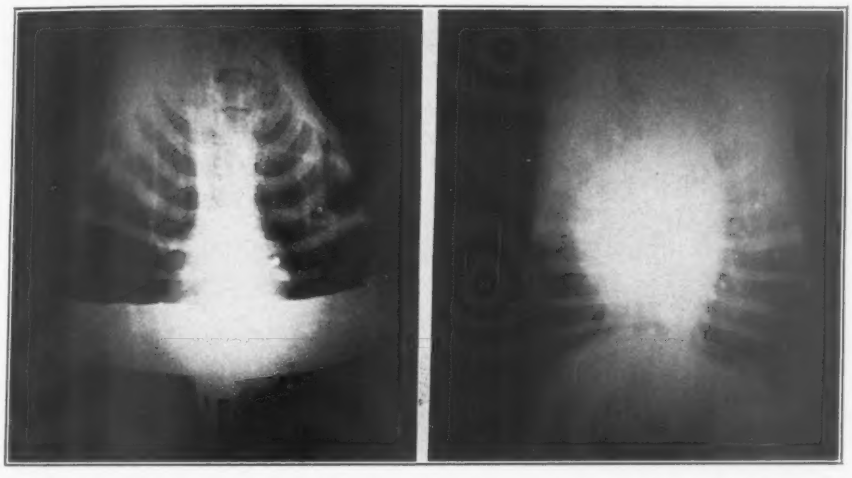

Fig. 10.—Figure on left shows x-ray appearance of heart with diminished negative intrapleural pressure. Figure on right shows dilatation of the right auricle with increased negative intrapleural pressures. Both plates were taken at the height of inspiration without changing the position of the tube.

The metal band seen in the left hand figure was not removed before taking the x-ray. This apparatus was frequently used to hold the needles in their proper position in the intrapleural spaces.

only produce mechanical effects, but these in turn involve chemical changes which react on the vital centers, and these produce reflex changes in the mechanics of the circulation. A detailed discussion of the chemistry of the blood in relation to altered peripheral resistance, respiration, etc., will be reserved for a separate communication.

Some of the important mechanical factors in relation to obstruction of the trachea and bronchi will be considered first. When there is obstruction to the inlet of air a reduction of pressure must occur in the intrapleural spaces, since the chest wall and diaphragm move away from the lung faster than the lung is able to follow them. Where the obstruction exists in the trachea above the bifurcation, the resulting re-

duction of intrapleural pressure will be approximately equal on both sides. If, however, the obstruction is in the right bronchus, then a greater reduction of pressure will occur in the right intrapleural space than on the left, although there will be some abnormal pressure on the left side as well.

This, we believe, may be explained by the fact that the mediastinum in the dog is very mobile, and the heart is displaced toward the obstructed side. This results in an abnormal stretch or pull of the opposite lung. The overstretching of the elastic tissues produces an in-

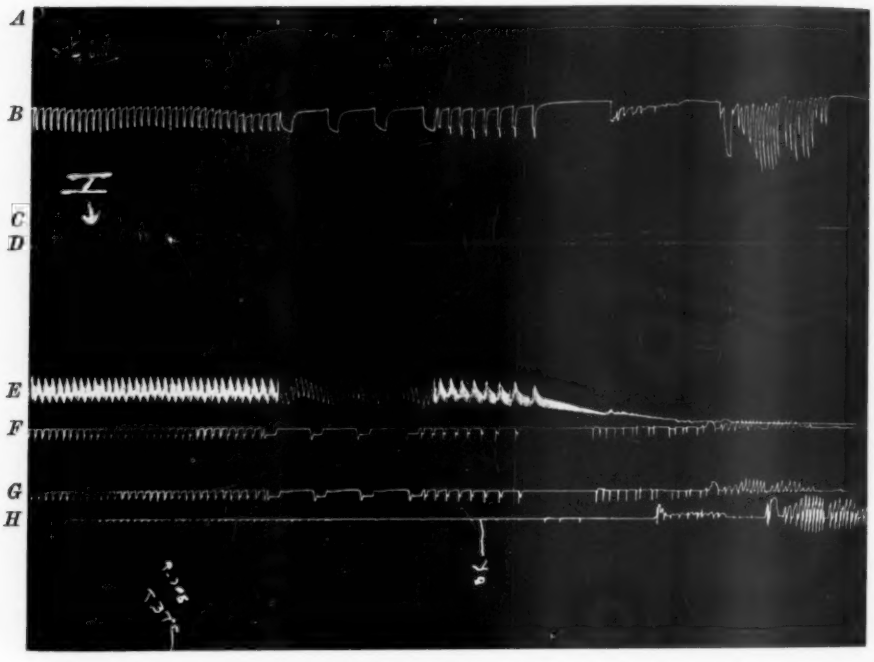

Fig. 11.—*A* represents time intervals; *B*, excursions of the chest wall; *C*, venous pressure tracing; *D*, base line for estimation of venous pressure changes; *E*, carotid blood pressure tracing; *F*, and *G*, intrapleural pressure readings; *H*, intratracheal pressure.

Note the respiratory waves in the venous pressure tracing at I. Pressure falls with inspiration and rises with expiration. With cessation of respiration these entirely disappear, although the heart is still beating. With artificial respiration they are also practically absent. Note the rise of venous pressure with cessation of respiration and gradual fall after death. This record shows particularly well the fall of blood pressure occurring with inspiration and the rise with expiration. With increasing degrees of obstruction this effect becomes even more marked. Since expiration is more forceful than normal, this also tends to produce a rise of systolic pressure.

creased separation of the lung from the chest wall. In both these instances, but more strikingly shown where the obstruction affects the trachea, there will be a diminished excursion of both the chest wall and diaphragm. This may be explained by the obstruction to inlet, the muscular effort being largely expended in reducing the pressure within the intrapleural spaces and lung itself.

This change is readily shown in the experimental record by reference to charted movements of the chest wall and diaphragm. Expiration becomes more forceful, due to the sudden release of active inspiration, in the presence of an abnormally negative intrathoracic pressure. These same pressure changes produce marked alterations in the pulmonary circulation as well as in the filling and function of the heart. Let us first consider the mechanical factors in relation to the heart itself. As the intrapleural pressure is rendered more negative a larger return of venous blood to the heart occurs, due to the reduction of pressure within the great veins of the thorax and the stretching of the heart itself during inspiration. The same reduction in pressure also increases the work of the heart not only by increasing the blood volume but also by throwing an additional load on ventricular and auricular contraction during inspiration, as the heart in this case must contract against an outside reduction of pressure tending to dilate it, in addition to the increased volume (Fig. 11). In this way, where there is sufficient obstruction of the trachea, it is relatively easy to produce an actual dilatation of the heart with insufficiency of the valves and death.

Important changes also occur in the pulmonary circulation with obstruction. Not only is there a reduction of pressure within the intrapleural spaces but also within the trachea, bronchi, and alveoli. Since the excursions of the chest wall and diaphragm are diminished with obstruction, it is obvious that the vessels coursing within the lung will not be elongated or stretched out as much as under normal conditions. Then, too, the reduction of pressure within the alveoli themselves tends to produce a dilatation or increased size of the vessels. This reduction in pressure within the alveoli will also effect the exchange of gases in the blood. As there is also some obstruction to expiration, there will be an added tendency for carbon dioxide to accumulate in the alveoli.

This increase in CO_2 will still further tend to increase the permeability of the capillaries and will contribute to the diminished flow of blood through the pulmonary circuit. The increased tortuosity and dilatation of vessels will result in a larger number of red cells flowing through the center of the vessels without actually coming in contact with the alveolar air. One must also consider that in extreme degrees of obstruction there may be a considerable reduction of available oxygen within the lung, and as a direct result of this, carbon dioxide will tend to accumulate within the alveoli and blood. Depth and rate of inspiration are increased through stimulation of the respiratory center, and the blood pressure is elevated through stimulation of the vasoconstrictor center.

The increased inflow of blood resulting from the diminished intrapleural pressure in the presence of obstruction results in an overfilling of the right auricle. A large volume of blood flows into the right ven-

tricle and with the contraction of the ventricle a considerable increase of peripheral resistance is encountered in the pulmonary circuit due to the facts previously described, i.e., diminished chest excursion, tortuosity of vessels, and dilatation of the capillaries. This results in a reflex slowing of the heart, allowing a longer recuperative or rest period.

Where the trachea is widely opened the intrapleural pressure is greatly diminished, in many instances being so nearly atmospheric that it was just recordable. In this instance the excursions of the chest wall and diaphragm are increased. The lung capillaries are well stretched out, and the velocity flow through the pulmonary circuit is increased. In this case more red cells are in contact with the capillary walls and the exchange of gases is thereby facilitated within the alveoli. There is also an adequate air supply present within the lung at approximately atmospheric pressure. The amount of blood returning to the heart is diminished, since there is less negative pressure acting on the great veins and heart. The cardiac contractions are also facilitated by the rise of pressure in the intrapleural spaces and the lung itself.

The diminished inflow, plus the squeezing action of the completely expanding lungs, results in a rise of venous pressure, fall of blood pressure, and increase of heart rate. The fall is still further aided by the increased oxygenation with relaxation of small arterioles in the periphery. As a result of the diminished venous return, the pressure in the veins within the abdomen gradually rises, and a great deal of blood may thus be lost to the general circulation by a pooling within the abdominal viscera.

This, we believe, accounts for the increased amount of blood found in the liver and kidney, and the relatively avascular conditions of the extremities in the experimental animal subjected to relatively low intrapleural pressure.

All of the above factors tend to produce a fall of body temperature, i.e., since more heat is lost through the lungs by increased pulmonary ventilation, as well as by radiation and conduction in the periphery due to the relaxation of surface vessels. This is in sharp contrast to the experiments in which the intrapleural pressure was rendered more negative, as in this instance the mechanism for normal heat loss is greatly interfered with.

The pulmonary ventilation is decidedly decreased, so that normal oxygenation and heat loss cannot occur in the lungs. Then, too, the increased carbon dioxide content of the blood produces a vasoconstriction of the peripheral vessels which seriously interferes with heat loss by radiation and conduction in the skin. In many dogs the body temperature rose to 103°-107° F. during the course of the experiment. This was most noticeable in experimental pneumonia. When the trachea

is widely opened, we have repeatedly noted a sharp fall in temperature. This occurs quite rapidly and is associated with excellent peripheral oxygenation, diminished intrapleural pressures, etc.

In general, it may be stated that variations of intrapleural pressure promptly affect the blood pressure. If the size of the tracheal inlet is decreased, the intrapleural pressure becomes more negative. Oftentimes the decrease is almost proportionate to the reduction of the inlet, i.e., if the size of the tracheal inlet is decreased from one-quarter inch to one-eighth inch, the intrapleural pressure is rendered almost doubly negative. This reduction of intrapleural pressure very promptly affects the filling and function of the right heart, and these volume changes, together with changes in velocity flow through the pulmonary circuit, produce prompt variations of the blood pressure, venous pressure, and pulse rate.

To be sure, reflex changes occur, affecting both the heart and the peripheral vessels, which further complicate the study; e.g., the increasing CO_2 concentration acts locally to cause relaxation of vessels within the lung and increase the permeability of the capillaries. Centrally, it acts upon the higher centers, producing increased rate and depth of respiration from stimulation of the respiratory center. The vasoconstriction center is also stimulated by the increase of CO_2, and this produces a rise of blood pressure by increase of the peripheral resistance. It is also possible that the carotid sinus may bear some direct relation to the production of the increased blood pressure.

Where the trachea is widely opened the amount of CO_2 in the blood is diminished. There is less stimulus to the respiratory center. The intrapleural pressure rises, i.e., becomes less negative, and there is relaxation of the peripheral vessels. The rise of intrapleural pressure diminishes the inflow of blood into the heart and blood tends to collect on the venous side. The diminished effective blood volume thus soon results in a rise of pulse rate and fall of blood pressure, and the increased flow through the lungs and skin results in a fairly rapid fall of body temperature.

SUMMARY

Experiments have been carried out on the dog showing the effects of increased and decreased intrapleural pressure upon the heart, blood pressure, and pulmonic and peripheral circulation.

It has been demonstrated that rendering the intrapleural pressure more negative produces dilatation of the heart, a diminished rate of flow through the pulmonary circuit with a relative anoxemia, a slow pulse, an increased blood pressure, fall of venous pressure, and rise in body temperature.

Rendering the intrapleural pressure less negative, i.e., more nearly atmospheric, results in a fall of blood pressure, rise of venous pressure,

increased pulse rate, relatively small heart, a lowered body temperature, and an increased rate of flow through the pulmonary circuit with increased oxygenation.

An instrument has been devised for recording graphically changes in venous pressure.

The writers wish to express their appreciation to Dr. Elliott C. Cutler for his many helpful suggestions and his friendly criticism throughout the experimental work.

They also wish to acknowledge their appreciation to Eli Lilly and Company of Indianapolis, Indiana, for their generosity in establishing a grant which enabled them to carry out the initial part of the research problem.

DEFORMITY OF THE CHEST ASSOCIATED WITH EXTREME DILATATION OF THE LEFT AURICLE. REPORT OF TWO CASES*

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SOME degree of dilatation of the left auricle is present in most patients with mitral disease, and extreme dilatation has been described in a number of cases and is now generally recognized as presenting a characteristic x-ray picture. In the more advanced stages such dilatation may cause symptoms: dysphagia from pressure on the esophagus; cough, dyspnea, hemoptysis, atelectasis or recurring attacks of bronchitis from pressure on the trachea or bronchi; or hoarseness from pressure on the recurrent laryngeal nerve. In some cases the symptoms have been so troublesome that operation has been performed—gastrostomy for a supposed carcinoma of the esophagus[1] or thyroidectomy.[2] Needless to say, surgical intervention failed to relieve the symptoms. Because the left auricle is situated posteriorly its enlargement, when this is sufficient to give signs, is marked by physical signs over the back —on the left, the right or on both sides—and in the right axilla. The most characteristic of these signs are dullness or dull tympany in one or both interscapular regions associated with diminished breath sounds and clearly transmitted heart sounds and murmurs and, when dilatation is extreme, a palpable systolic impulse in the right axilla. These signs may be difficult to interpret and a mistaken diagnosis of hydrothorax has led to tapping of the right chest.[3, 4] Post-mortem examination showed that the blood which was obtained came from the left auricle, an observation that seems almost incredible until we realize that the capacity of the left auricle in such cases has been reported as 1,760 c.c.,[5] two liters,[6] two and one-half liters,[7] three liters,[8] and forty ounces after fixation.[4]

At the New York Hospital two patients have recently been under observation who have shown evidence of extreme dilatation of the left auricle and also a deformity of the chest wall, not merely a bulging of the precordial area which is seen in so many patients with large hearts or an asymmetry of the nipples as has been described by Schwartz[9] in cases of mitral disease, but a great increase in the anteroposterior diameter of the thorax, appearing as if the sternum and the vertebral column had been pushed apart. In one case the increase in the depth of the chest was followed over a period of five years until the antero-

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posterior diameter at the level of the fourth thoracic spine actually exceeded the transverse diameter by three centimeters, and this progressive change in the shape of the chest was believed to result from the great increase in the anteroposterior diameter of the heart. As far as can be determined this particular deformity of the chest has not received special attention. In most of the reported cases of extreme dilatation of the left auricle no mention is made of the shape of the chest. Parkinson,[10] however, remarked that the chest of his patient, a young man aged twenty-two years who had had dyspnea for ten years and who was found to have a remarkably dilated left auricle, was unusually deep.

REPORT OF CASES

CASE 1.—American housewife, aged thirty-seven years. This patient had chorea at seven years, occasional growing pains and frequent attacks of tonsillitis but no other illness. From the age of nineteen years she was short of breath on effort, and from the age of twenty-four years she was troubled by palpitation. When she was twenty-six years old, following unusual exertion, she had very severe and persistent dyspnea, palpitation and weakness. These symptoms persisted in spite of ten days' rest at home and led her to enter the New York Hospital (in October, 1919). At this time it was noted that she was poorly developed and nourished, dyspneic and cyanotic. The apex impulse was at the anterior axillary line; the heart rate was rapid and the rhythm totally irregular; a long rumbling diastolic murmur was heard. With rest and digitalis the patient improved and was discharged after one month. The record of this admission contains no detailed description of the shape of the chest or of the signs over the lungs.

For the next ten years the patient attended the out-patient department and took enough digitalis to control her ventricular rate. During this time she was somewhat dyspneic but was able to do clerical work for seven years, and after her marriage at thirty-three years to do her housework without undue fatigue. She never became pregnant.

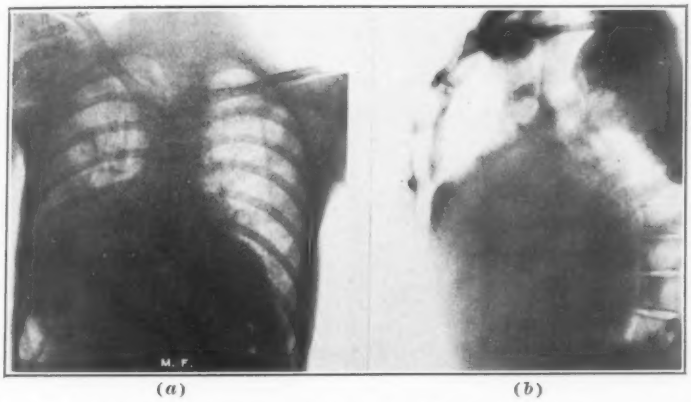
In March, 1929, she was readmitted to the hospital because of nervousness and palpitation of two months' duration. The diagnosis at this time was rheumatic heart disease, mitral stenosis and insufficiency, enormous dilatation of the left auricle and auricular fibrillation. Shortly after her admission the following note was made by Dr. Conner: "Patient has the very small slender frame with poor musculature seen in so many women with mitral stenosis. Striking change in configuration of chest with increase in the anteroposterior diameter. Orthopnea, some cyanosis of lips and cheeks. Apex beat very diffuse but felt best in the sixth space in the anterior axillary line. Dullness 4.5 cm. to right and 10 cm. to left. Sharp systolic impulse followed at apex by diastolic thrill; no pulsation or thrill at base. Apical first sound very sharp and followed by a loud systolic murmur, a faint second sound and an early diastolic rumble. No distinct accentuation of P_2. In right axilla a faint but distinct systolic impulse is felt, and the two heart sounds are heard faintly. Action fairly slow and totally irregular. Over right lung in front percussion note distinctly hyperresonant as far out as anterior axillary line where dull tympany is heard, becoming *dull* in midaxilla. Behind, moderate impairment of resonance in interscapular region and below angle. Over this region vesicular murmur is very much less distinct than on left side. Exaggerated vesicular murmur in front." The liver and spleen were not palpable and there was no edema.

The x-ray films (Fig. 1) showed enormous dilatation of the left auricle, and on fluoroscopic examination the barium-filled esophagus was seen to curve backward

around the auricle. There was no delay in the passage of barium through the esophagus. Electrocardiogram showed right axis deviation and some slurring of QRS. Blood pressure was approximately 140/60 mm. Hg. Blood Wassermann reaction was negative; blood count showed slight secondary anemia. Urine showed an inconstant trace of albumin.

After a month in the hospital the patient returned to her home, remained in her usual health for six months and then died rather suddenly. The exact mode and cause of death could not be ascertained.

CASE 2.—A schoolgirl, native born of German parents, was under observation from the age of thirteen years until her death at nineteen years. At the age of four years she had a febrile attack with joint pains, called "grippe." At the age of eight years she had pertussis and at that time was said to have heart trouble. She had no other rheumatic attacks, no chorea, no tonsillitis, indeed no acute illness. When she was thirteen years old, it was noted that she had signs of mitral stenosis and an unusually large heart. A few months later the rhythm became totally irregular, and the patient was admitted to the New York Hospital (in November, 1924).



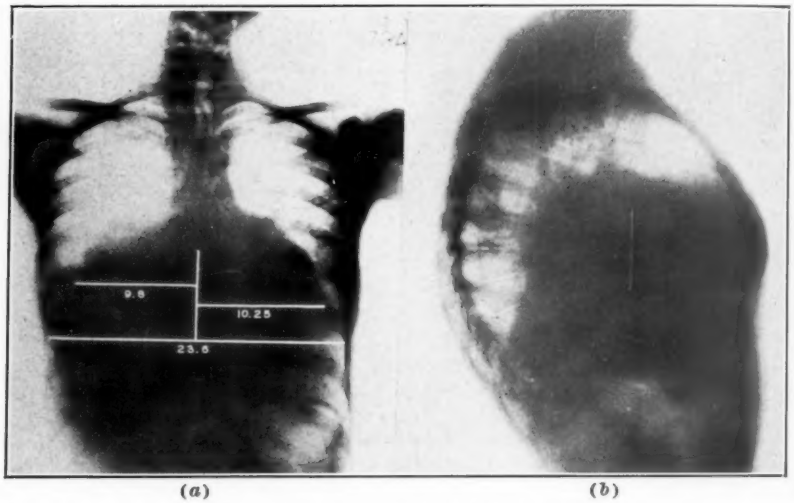
(*a*) (*b*)

Fig. 1.—Case 1. Teleroentgenograms taken in March, 1929.
(a) Anteroposterior view showing the great cardiac enlargement with the shadow of the left auricle extending to the right of the heart almost to the chest wall.
(b) Lateral view showing the large heart filling the space between spine and sternum and the increased depth of the chest.

At this time the apex impulse was in the sixth space and the cardiac borders, as determined by percussion and by x-ray examination, extended 10 cm. to the left and 6 cm. to the right of the midline. The rhythm was irregular. The first sound at the apex was sharp and was preceded by a rumbling diastolic murmur. Electrocardiogram showed auricular fibrillation, right axis deviation and no abnormality of the ventricular waves. Quinidine restored sinus rhythm temporarily, but fibrillation promptly reappeared, and the patient was discharged on maintenance doses of digitalis. In June, 1925, she stopped taking digitalis and was readmitted to the hospital because of cardiac decompensation. The heart was slightly larger than it had been nine months earlier, but there were no new findings. After a month in the hospital the patient was sent to a convalescent home, and in November, 1925, she was admitted to the children's cardiac clinic. She attended this clinic irregularly until her death in January, 1931. A Christian Scientist, she "did not believe in taking medicine," and for weeks at a time omitted the digitalis or took less than

the dose ordered with the result that her ventricular rate was rapid much of the time. During these years she attended school and later a workshop for Class II cardiac patients; she helped with the housework and from time to time she experimented with various outside activities such as dancing and working as clerk in a shop during afternoon and evening hours. She was always short of breath on exertion and always unwilling to curtail her activities. Apart from an occasional cold or mild attack of bronchitis she had no illnesses; she had no edema of the ankles, no swelling of the liver or other evidence of congestive heart failure; she never complained of hoarseness or of dysphagia.

During the years that she was under observation there was an interesting and progressive change in the physical signs. In 1924, she was a flat-chested little girl; in 1926, she looked "round-shouldered," and it was noted that this appearance was caused by an increase in the anteroposterior diameter of the chest. This increased until it exceeded the transverse diameter. In March, 1928, the apex impulse was in the sixth space in the midaxillary line; dullness extended from the left axilla to



(*a*) (*b*)

Fig. 2.—Case 2. Teleroentgenograms taken in March, 1928.
(a) Anteroposterior view showing the characteristic shape and enormous size of the heart. The haziness of the right costophrenic angle is due to the breast shadow.
(b) Lateral view showing the great increase in the distance between sternum and vertebral column.

6 cm. to the right of the midline. Over the right chest there was dull tympany anteriorly and posteriorly with dullness in the axilla, where in the fourth and fifth spaces there was a distinct systolic impulse, easily palpable and recorded on polygraphic tracing. At the apex the first sound was sharp, preceded by a diastolic rumble and followed by a systolic blow; the second sound was tapping. At the base the second pulmonic sound was accentuated. The heart sounds and murmurs were heard over the left chest posteriorly and in the right axilla. Fluoroscopic examination showed a greatly enlarged heart with the shadow of the left auricle extending backward, as seen in the first oblique position, and to the right almost to the chest wall. A year later the anteroposterior diameter of the chest, as measured with a pelvimeter, exceeded the transverse diameter; cardiac dullness extended 4 cm. to the left in the second space and reached the midaxilla in the fifth and sixth spaces; on the right it extended 6 cm. in the second space, 8 cm. in the third, 9 cm. in the

fourth and to the axilla in the fifth. There was also dullness in the third and fourth spaces in the right axilla with dull tympany in both interscapular regions and at both bases posteriorly. Over the area of dull tympany the breath sounds were diminished and the heart sounds were heard. There was little change in the patient's condition until the fall of 1930 when, owing to unusual stress at home, she became exhausted and had increased dyspnea. Late in December she caught cold and had a very troublesome cough. This cough kept her awake most of one night, and the next day she became acutely dyspneic and cyanotic and died rather suddenly. On the day of her death the heart signs were as they had been except that the rate was very rapid; bubbling râles were heard over the entire chest; there was no edema of the extremities. An autopsy was not permitted.

COMMENT

In each of these cases the most striking feature of the physical examination was the great increase in the anteroposterior diameter of the chest, and, in the absence of other factors which might explain this

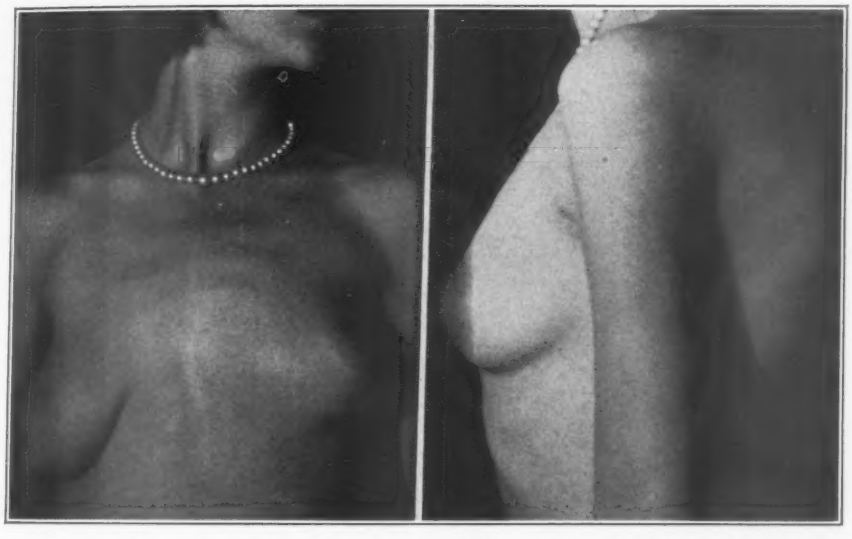


Fig. 3.—Case 2. Appearance of patient in October, 1930. Note the bulging of the precordial area, the asymmetry of the breasts, the poor muscle development and particularly the increase in the anteroposterior diameter of the chest.

deformity, it was believed that the change in the contour of the chest was secondary to the great enlargement of the heart. The change in the shape of the chest was so remarkable that for a period of about two years every child attending the children's cardiac clinic at the New York Hospital was examined for chest deformity, and in most cases measurements of the anteroposterior and transverse diameters were made and recorded. Many children showed asymmetry, bulging of the precordial area or old rachitic deformities, but no other case showing any such increase in the anteroposterior diameter as is described here was discovered. Nor was there discovered another case of extreme dilatation of the left auricle.

In reviewing the reported cases of extreme dilatation of the left auricle it would seem that the usual factors responsible for this condition are an incompetent mitral valve, disease—probably rheumatic in most cases—of the wall of the left auricle with subsequent fibrous replacement of muscle tissue, auricular fibrillation and a forceful left ventricle. Usually there is a rheumatic history but not a history of repeated rheumatic episodes with progressive cardiac damage, and in most cases the functional capacity of the patient has been remarkably good for a number of years, indicating that the left ventricle was sufficiently forceful to maintain fair compensation in spite of great mechanical disadvantages. Under these circumstances the left auricle becomes an enormously dilated sac filling the retrocardiac space and extending to the left and right. With each systole this sac transmits the force of the left ventricle, a pressure of perhaps 120 mm. Hg or more. If the conditions occur in a young person with an elastic chest, this expansile pulsation might easily force the sternum and the spine away from one another and so cause the deformity here described. This deformity may be an advantage in that the great increase in the anteroposterior diameter of the chest may explain the absence in these patients of the pressure symptoms commonly associated with extreme dilatation of the left auricle.

SUMMARY

Two additional cases of extreme dilatation of the left auricle are reported. In history, physical signs and x-ray findings these closely resemble the other cases reported in the literature.* They are remarkable, however, in that each showed a pronounced change in the configuration of the thorax. This change was believed to be secondary to the enlargement of the heart, the result of pressure exerted by the left ventricle through the dilated left auricle. It is believed that the increased depth of the chest explains the absence of those pressure symptoms which are often associated with extreme dilatation of the left auricle.

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*No attempt is made to summarize the literature on the subject of extreme dilatation of the left auricle. Reports of cases may be found in the works aleady cited as well as in the articles by Bramwell and Duguid[11], Bedford[12], Lutembacher[13], and others, and from these papers a bibliography of the more noteworthy cases may be assembled. Other cases have been reported by men whose interest was in the pressure symptoms rather than in the heart, and doubtless many cases have been seen but not recorded in print.

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ON THE SIGNIFICANCE OF THE JUGULAR PULSE IN THE CLINICAL DIAGNOSIS OF VENTRICULAR TACHYCARDIA*

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PAROXYSMAL ventricular tachycardia is not so rare as was formerly supposed. Since 1909, when Lewis[1] reported the first case, about seventy acceptable cases have been described. It is important to differentiate ventricular from auricular tachycardia because of the difference in prognosis and treatment. Paroxysmal auricular tachycardia is often a mild functional disorder without underlying cardiac disease. Although ventricular tachycardia may also occur in the absence of severe cardiac disease, it is usually associated with grave cardiac disease. The average duration of life in four-fifths of sixty-five cases of paroxysmal ventricular tachycardia collected by Strauss[2] was only twenty-four days.

ELECTROCARDIOGRAPHIC AID IN DIAGNOSIS

Most writers have considered an electrocardiogram indispensable for the diagnosis of ventricular tachycardia. The generally accepted criteria for diagnosis are outlined below:

1. The complexes must be of the ventricular form, i.e., similar to a ventricular premature beat and distinctly abnormal in form. Lewis has shown that this alone is insufficient for the diagnosis, as aberrant ventricular complexes may follow impulses arising in the auricles or junctional tissues, especially if the rate is increased.

2. Evidence of auricular activity occurring at a rate different from that of the ventricle is sufficient to make the diagnosis.

3. The onset of a paroxysm without evidence of auricular activity, preceding the first ventricular complex, is diagnostic.

4. A tachycardia of the ventricular form which occurs in the presence of long-standing auricular fibrillation is good evidence for the diagnosis.

The first criterion mentioned above must always be present and must be supplemented by one of the others. A presumptive diagnosis may be made (1) if the termination of the paroxysm is followed by a compensatory pause identical with that found after a ventricular premature beat, or (2) if ventricular premature beats of similar form to

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ventricular complexes seen in the paroxysm have been found, or (3) if the ventricular rate varies slightly.

CLINICAL DIAGNOSIS

Strong and Levine[3] and Levine[4] pointed out that in some cases a clinical diagnosis of ventricular tachycardia can be made. They found that in ventricular tachycardia the first cardiac sound varied in intensity in definite cycles and that there was a slight irregularity in rate; in auricular tachycardia, on the other hand, the sounds were of equal intensity and occurred at regular intervals. Levine suggested that the variations might be due to auricular activity. Moreover, pressure on the vagus, carotid sinus, or eyeballs, which has been found ineffective in ventricular tachycardia, often altered auricular tachycardia. With these criteria, Levine made the correct clinical diagnosis in several cases.

In 1923, Gallavardin[5] took a jugular pulse tracing simultaneously with an electrocardiogram in a case of paroxysmal ventricular tachycardia. He was surprised to find regular venous waves occurring at a rate less than half of the ventricular rate. These waves varied in intensity without relation to respiration. He recognized the clinical value of this observation and stated that if a jugular tracing or inspection of the jugular veins showed a recurring impulse coming at a rate about half that of the arterial rate, and if the pulsations showed variations in intensity not related to respiration, a diagnosis could be made of paroxysmal ventricular tachycardia with conservation of the normal auricular rhythm. In his later papers no further mention is made of the use of this sign clinically.

Allan[6] and Fischer[7] also have published tracings of the jugular pulse with simultaneous electrocardiograms in cases of ventricular tachycardia which likewise showed a slower auricular rate as manifested by the jugular pulse tracing. However, these authors failed to stress this slower jugular pulse rate as a useful clinical sign.

In view of our findings in the following case and of a review of the reported cases of proved ventricular tachycardia, it is proposed that a jugular pulse rate slower than that of the ventricles represents a sign by which a positive clinical diagnosis can be made in many cases. The mechanism of this sign is well known, but its clinical value has not been generally appreciated. It is recognized that during ventricular tachycardia the auricles may be beating independently or that retrograde rhythm may be present with or without block. If the auricular rate is slower than the ventricular rate, pulsations at this slower rate should be visible in the jugular vein. That is, the jugular pulse rate will be slower than the apical or radial rate.

Two factors serve to make the jugular pulsations prominent: first, the venous pressure is usually increased in ventricular tachycardia;

and second, since the ventricles are beating so much faster, the right auricle will frequently be contracting against a closed tricuspid valve, thus causing stasis waves in the great veins. The diagnostic value of the jugular pulse in ventricular tachycardia was noted in the following case.

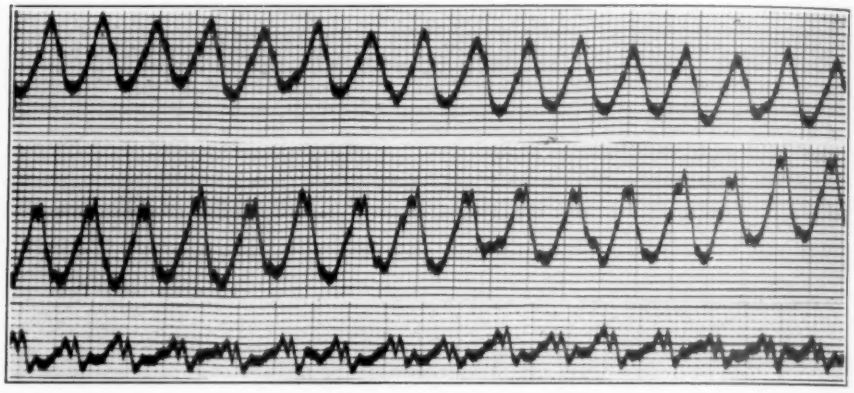

Fig. 1.—Electrocardiogram showing Leads I, II and III respectively. Definite evidence of auricular activity cannot be made out.

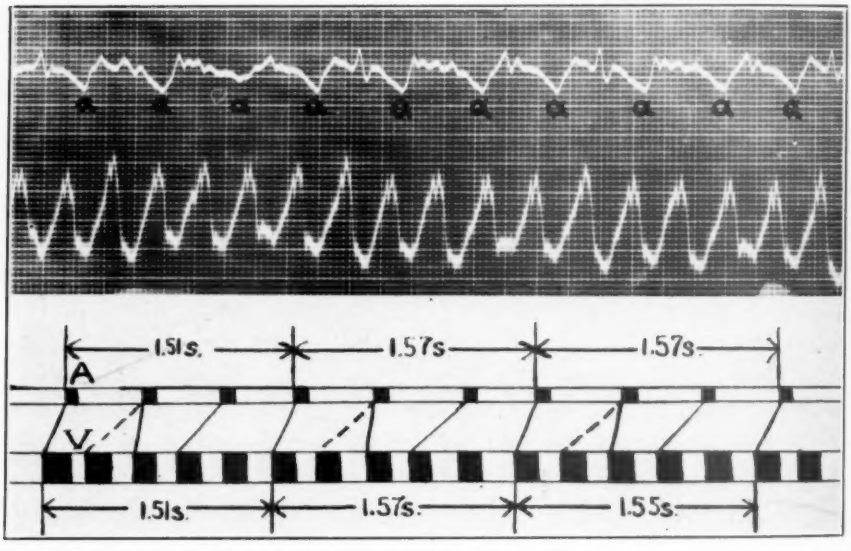

Fig. 2.—Simultaneous jugular pulse tracing and electrocardiogram (Lead II). The jugular tracing is inverted so that a-waves are negative. Auricular complexes cannot be made out definitely in the electrocardiogram.

The diagram indicates the ventriculo-auricular rhythm (retrograde conduction with 5:3 block). The auricular beats are shown in strip A, each beat corresponding with the beginning of an a-wave in the jugular tracing. The ventricular beats, corresponding with the onset of the ventricular complexes in the electrocardiogram, are shown in strip V. The solid oblique "tie" lines show unblocked impulses passing from ventricle to auricle (the dotted "tie" lines indicate alternate possibilities). The ventricular rate shows a slight irregularity. The auricular rate shows a definite irregularity which repeats itself every three beats, and the period occupied by three auricular beats corresponds, throughout, almost exactly to the period occupied by five corresponding ventricular beats.

CASE REPORT

A thirty-four-year-old male* entered the University of California Hospital with an obvious paroxysmal tachycardia which had started four hours before. He had enjoyed comparatively good health except for numerous similar attacks in the previous four years. On examination, the patient was seen to be cyanotic and orthopneic. His heart was slightly enlarged to the left and was beating with an apical rate of

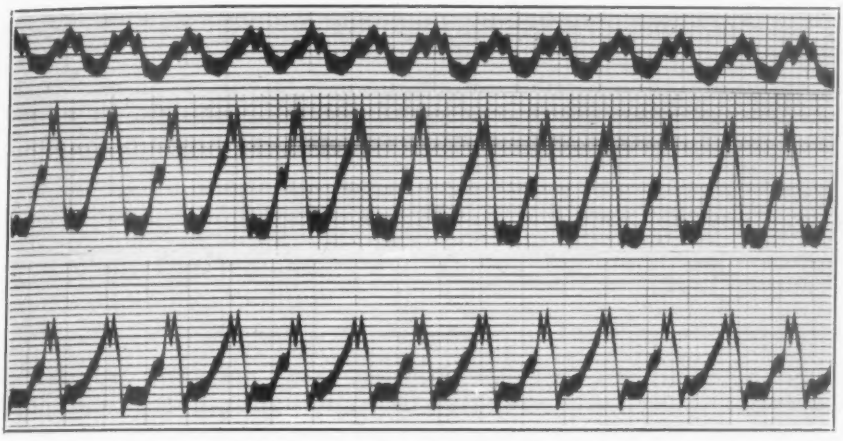

Fig. 3.—Electrocardiogram showing Leads I, II and III taken at another time. Evidence of auricular activity occurring on alternate ventricular complexes is clearly shown in Leads II (probable retrograde conduction with 2:1 block).

Fig. 4.—Electrocardiogram showing Leads I, II and III respectively after the tachycardia.

about 195 per minute. No irregularity in time or intensity of the first sound was detected. The jugular bulb and vein were pulsating distinctly at a rate of 115 per minute. The pulsations were obviously stasis waves and the veins were full even in the upright position. Since the ventricles were beating more rapidly, these waves were assumed to be due to auricular activity at a slower rate. This could not occur in auricular tachycardia, and therefore a diagnosis of ventricular tachycardia

*This patient was Case 1 in the report by Sampson and Anderson[8] on the treatment of cardiac arrhythmias with potassium salts.

was made. The electrocardiogram (Fig. 1), which showed a slight irregularity in rate, did not show evidence of auricular activity (P-waves) at this time, and therefore a positive diagnosis by this means was not possible. The jugular pulse tracing (Fig. 2) showed definite a-waves occurring with an irregularity which repeated itself every three beats. The period occupied by each three auricular beats was of the same length as the period occupied by five ventricular beats. In other words, as shown by the diagram, a retrograde rhythm with a net 5:3 block was present. At this time, therefore, the jugular pulsations were necessary to make a definite diagnosis of ventricular tachycardia, which would have been impossible to make from the electrocardiogram alone. At another time an electrocardiogram (Fig. 3) of this patient did show evidence of auricular activity at a rate slower than the ventricular rate (probable retrograde rhythm with 2:1 block). Fig. 4 shows the electrocardiogram of this patient following the tachycardia.

LIMITATIONS OF THE SIGN

This sign, the slower jugular pulse, has definite limitations which, fortunately, can be determined at the present time by a review of the reported cases. The sign is valueless in cases with coexisting auricular fibrillation; in cases in which the auricles are beating as rapidly as the ventricles (only one such proved case on record, [Scott]); and in the rare case of nodal tachycardia* in which this sign might also be present. The sign would be valuable, however, in many instances (as in the case reported) when the electrocardiogram fails to show evidence of slower auricular activity, and when, as is usually the case, the onset of the paroxysm is not recorded. In these cases a clinical diagnosis might be made which would be impossible to make from the electrocardiogram alone. If, as Levine suggests, irregularities in the first cardiac sound are due to auricular activity, the same limitations would apply to his sign.

ANALYSIS OF CASES

Including our own, we have analyzed sixty-eight reported cases of proved paroxysmal ventricular tachycardia, which are tabulated in Table I with respect to the state of the auricles. A number of cases, many of which might have been paroxysmal auricular tachycardia with aberration of the ventricular complexes, were rejected as not fulfilling the criteria outlined above.

Of the sixty-eight cases there were ten diagnosed by recording the onset of the paroxysm, in which the state of the auricles could not be determined. Of the remaining fifty-eight, auricular fibrillation, or occasionally flutter, was present in twenty-one. Of the remaining thirty-seven, there was only one case of ventricular tachycardia with a retrograde 1:1 rhythm. An independent auricular rhythm was present in twenty-five cases, and eight cases showed retrograde rhythm with partial block. Three cases showed auricular complexes occurring more slowly

*So far as known, ventricular tachycardia cannot be distinguished from nodal tachycardia with aberration of the ventricular complexes.

TABLE I

	RHYTHM OF AURICLES					
	FIBRILLATION OR FLUTTER	RETROGRADE 1:1 RHYTHM	RETROGRADE RHYTHM WITH PARTIAL BLOCK	INDEPENDENT RHYTHM	AURICULAR RHYTHM UNKNOWN THOUGH P-WAVES ARE SEEN	NO P-WAVES MADE OUT
Allan, Geo. A.: Glasgow M. J. **107**: 74, 1927.			1			
Anderson, M. C.: Am. J. M. Sc. **181**: 369, 1931.				1		
Barrier, C. W.: J. A. M. A. **89**: 742. 1927.				1		
Butterfield, H. G., and Hunt, G. H.: Quart. J. Med. **7**: 209, 1914.				1		
Clarke, R. Manning: Calif. & West. Med. **32**: 252, 1930.					1	
Cohn, Alfred E.: Am. J. M. Sc. **151**:						
Eakin, W. W.: Canad. M. A. J. **51**: 1454, 1926.				1		
1926.					1	1
Felberbaum, David: Am. J. M. Sc. **166**: 211, 1923.						1
Fischer, Robert: Wien. Arch. f. inn Med. **14**: 405, 1927.				1		
Gallavardin, Louis: Arch. des mal du coeur **13**: 121, 1920.				1		
Ibid.: **13**: 207, 1920.	1					
Ibid.: **13**: 210, 1920.	1					
Ibid.: **15**: 298, 1922.				1		
Ibid.: **19**: 153, 1926.	2					1
Gilchrist, A. R.: AM. HEART J. **1**: 546, 1925-26.	1			2		1
Hart, S. T.: Heart **4**: 128, 1912-13.			1			
Hollingsworth, E. W.: Ann. Int. Med. **5**: 1506, 1931-32.				1		
Jones, T. D., and White, P. D.: AM. HEART J. **2**: 139, 1926-27.				1		
Kerr, W. J., and Bender, W. L.: Heart **9**: 269, 1921.	1					
Levine, S. A., and Curtis, A. N.: AM. HEART J. **1**: 413, 1925-26.	1					
Levine, S. A.: AM. HEART J. **3**: 177, 1927-28.						1
Levine, S. A., and Fulton, M. N.: J. A. M. A. **92**: 1162, 1929.	1			2		
Levy, R. L.: Arch. Int. Med. **30**: 451, 1922.	2					
Lewis, Thomas: Lancet **1**: 382, 1909.				1		
Lewis, Thomas: Mechanism of the Heart Beat, London, 1911, p. 168.				1		
Luten, Drew: Arch. Int. Med. **35**: 74, 1925.				1		
Ibid.: **35**: 74, 1925.	2					
Marvin, H. M.: Heart **10**: 279, 1923.			1			
Marvin, H. M.: AM. HEART J. **4**: 21. 1928-29.	1			2	1	

TABLE I—CONT'D

	RHYTHM OF AURICLES					
	FIBRILLATION OR FLUTTER	RETROGRADE 1:1 RHYTHM	RETROGRADE RHYTHM WITH PARTIAL BLOCK	INDEPENDENT RHYTHM	AURICULAR RHYTHM UNKNOWN THOUGH P-WAVES ARE SEEN	NO P-WAVES MADE OUT
Marvin, H. M., and White, P. D.: Arch. Int. Med. **29**: 403, 1922.			1			
McMillan, T. M., and Bellet, S.: AM. HEART J. **7**: 70, 1931-32.				1		
Moore, H.: Irish J. M. Sc. **36**: 754, 1928.			1			
Orsi, A., and Villa, L.: Arch. d. mal du coeur **21**: 353, 1928.	1					
Porter, Wm. B.: J. Am. M. Sc. **167**: 821, 1924.				1		
Reid, W. D.: Arch. Int. Med. **33**: 23, 1924.				1		
Ritchie, W. T.: Edin. M. J. **33**: 193, 1926.						1
Robinson, G. C., and Herrman, G. R.: Heart **8**: 59, 1921.			2	1		
Schwenson, C.: Heart **9**: 199, 1921-22.	1					
Scott, R. W.: Heart **9**: 297, 1921.		1				
Singer, R., and Winterberg, H.: Wien. Arch. f. inn. Med. **3**: 329, 1922.						1
Strauss, M. B.: Am. J. M. Sc. **179**: 337, 1930.	2					
Strong, G. F., and Levine, S. A.: Heart **10**: 125, 1923.						1
Vaughan, W. T.: Arch. Int. Med. **21**: 381, 1918.						1
White, P. D., and Palmer, R. S.: AM. HEART J. **3**: 454, 1927-28.	1			1		
Willius, F. A.: Bost. M. & S. J. **178**: 40, 1918.						1
Willius, F. A.: Ann. Clin. Med. **3**: 537, 1925.				1		
Wolferth, C. C., and McMillan, T. M.: Arch. Int. Med. **31**: 184, 1923.	3			1		
Present case report.			1			
Total	21	1	8	25	3	10

Cases in which sign would be absent	22		
Cases in which sign should be present		36	
Cases in which status of sign is not known			10

than the ventricular complexes, though the exact auricular rhythm could not be determined. Thus in thirty-six out of the fifty-eight cases in which it was possible to determine the auricular rhythm, it should have been possible to diagnose ventricular tachycardia by the jugular pulse.

If the onset of the paroxysm had not been recorded, an accurate electrocardiographic interpretation would have been impossible in ten of

the reported cases. Moreover, in our case, it was not possible to make a positive diagnosis from the first electrocardiogram. Consequently, there are probably a number of cases of ventricular tachycardia which cannot be differentiated electrocardiographically from auricular tachycardia with aberration of the ventricular complexes.

The presence of jugular pulsations occurring more slowly than the apical rate would be a valuable aid in the diagnosis of such cases. However, a jugular pulse at the same rate as the apical rate would not rule out ventricular tachycardia, as a 1:1 retrograde rhythm might be present.

SUMMARY AND CONCLUSIONS

1. Paroxysmal ventricular tachycardia may often be differentiated clinically from auricular tachycardia when jugular pulsations at a slower rate than the apical rate are present.

2. A case is reported in which a diagnosis of paroxysmal ventricular tachycardia could not be definitely made from the electrocardiogram, but in which the diagnosis was made by the presence of jugular pulsations. It is suggested that there may be many similar cases in which this clinical sign alone could make a positive diagnosis, or in which it would be a necessary supplement to the electrocardiogram in diagnosis.

3. During ventricular tachycardia the most common auricular rhythms in the order of frequency are: an independent rhythm, auricular fibrillation, and retrograde rhythm with partial block.

4. The sign discussed in this paper has limitations but is applicable to about two-thirds of the reported cases. The coexistence of auricular fibrillation is the only important condition which renders the sign valueless.

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THE CREATINE CONTENT OF THE MYOCARDIUM OF NORMAL AND ABNORMAL HUMAN HEARTS*

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IT IS the general belief today that the immediate energy for the contractile process of skeletal muscle is derived from the breakdown of phosphocreatine.[1] This view has been extended recently by Clark, Eggleton and Eggleton[2] to include the contraction of cardiac muscle.

Because of the rapid breakdown of phosphocreatine after the death of a tissue, it is very difficult to study the concentration of this substance in human muscle. Creatine alone, however, is relatively stable and therefore can be estimated with little difficulty.

Skeletal muscle shows a decrease in creatine content in several pathological conditions accompanied by muscular weakness.[3-9] As Myers, in his recent review,[10] stated: "The potential muscular efficiency appears to depend upon the creatine content of the muscle. . . ."

The work herein presented was carried out to test whether this generalization would hold true in the case of the myocardium. Relatively few reports are available concerning the creatine content of the human heart, and these apparently deal only with the normal.

MATERIALS AND METHODS

Portions of left ventricular myocardium were obtained from 80 cases coming to autopsy at the University of Iowa Hospitals. These cases, although not consecutive, were not selected; the diagnosis in each case was unknown to me until after the analyses were completed and the results computed. Approximately the same part of the ventricle was used in each case in order to avoid possible errors due to differences in creatine content of the various parts of the musculature.

The following method of preparing the samples was adopted: The fresh piece of tissue was placed upon a piece of filter paper, and a rectangular block was cut from it entirely devoid of epicardium, endocardium, and papillary muscle. After this block had been blotted free of blood and moisture, its two ends were sliced off and discarded. Then it was divided into three approximately equal portions each of which had thus been dried to an equal degree. These portions were immediately placed in weighing bottles and weighed. Two were used for duplicate creatine analysis; the third was dried in an electric oven at 100° C. to constant weight.

Obviously this method of determining the water content may not allow accurate comparison of the water-solid ratio of two different hearts prepared separately; however, it does indicate accurately the water content of the pieces from the same block which were used for creatine determinations. Thus the creatine contents can be listed in comparable values.

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Creatine was measured as creatinine according to the method of Rose, Helmer and Chanutin,[11] and is reported in terms of creatine. There was an average difference of slightly more than 3 per cent between duplicates.

RESULTS

Of the 80 hearts used in this investigation, 48 are classified here as normal, 17 as decompensated hearts, and the remaining 15 fall into a miscellaneous group.

Normal Hearts

Included in this group are the hearts from patients with proved diagnoses of pneumonia, empyema, lung abscess, bronchiectasis, tuberculosis, carcinoma of the bronchus, pulmonary embolism, otitis media, mastoiditis, lateral sinus thrombosis, cerebral hemorrhage, skull fracture, brain tumor, meningitis, encephalitis, neurosyphilis, septicemia, carcinoma of various parts of the digestive tract, duodenal ulcer, intestinal obstruction, strangulated hernia, peritonitis, cholecystitis, toxic necrosis of the liver, pancreatitis, uremia, urinary tract infection, nephritis, carcinoma of the bladder, carcinoma of the cervix, carcinoma of the breast, carcinomatosis, actinomycosis, cellulitis, pemphigus, osteomyelitis, extensive burns, severe hemorrhage, pernicious anemia, diabetes, Hodgkin's disease, lymphoblastic lymphoma, and amyotrophic lateral sclerosis.

Strictly speaking, the hearts from many of these cases could not be called perfectly normal from an anatomical point of view. In fact, if all hearts showing slight cloudy swelling, slight brown atrophy, or sclerosis of the proximal coronary arteries were excluded from this normal group, only a few would remain. As it is, all hearts which gave no clinical symptoms, as far as could be ascertained from the records, were included in this group unless they presented rather marked gross or microscopic anatomical changes. The results of the analyses of the 48 normal hearts are summarized in Table I.

TABLE I

FORTY-EIGHT NORMAL HEARTS

	MEAN	STANDARD DEVIATION
Creatine, mg. per cent of moist weight	202	37
Water, per cent	79.17	1.04
Creatine, mg. per cent of dry weight	971	165
Comparable creatine,* mg. per cent	194	33

*The comparable creatine value is the creatine content of moist tissue based upon an arbitrary standard water content of 80 per cent. It is obtained by dividing the dry weight value by 5.

The standard deviation for the comparable creatine in this table indicates very good agreement among the individual samples. There were a few cases in this group, however, in which there was considerable

deviation from the mean. These cases are listed here in detail. Perhaps further work will indicate why they are so different from the rest in regard to creatine content.

SAMPLE NO.	DIAGNOSIS	COMPARABLE CREATINE, MG. PER CENT
7	Prostatic hyperplasia. Chronic bilateral ureteritis and pyelonephritis. Acute gangrenous cystitis. Acute uremia. Bronchopneumonia. Streptococcus septicemia.	117
63	Carcinomatosis: Breast, regional nodes, mediastinum, liver, retroperitoneal nodes, adrenals.	117
51	Malignant lymphoma, lymphoblastic type. Lateral sinus thrombosis. Septicemia. Secondary anemia. BMR = +20.9%. Heart: Some coronary sclerosis and brown atrophy.	134

Influence of Sex.—That there is no difference in creatine content of the heart of the two sexes is shown in Table II.

TABLE II

INFLUENCE OF SEX ON THE CREATINE CONTENT OF THE NORMAL HEART

SEX	NUMBER OF CASES	COMPARABLE CREATINE MG. PER CENT
Male	30	193
Female	18	196
Total	48	194

SAMPLE NO.	DIAGNOSIS	COMPARABLE CREATINE, MG. PER CENT
3	Cellulitis, right arm. Streptococcus septicemia. General sepsis. Bronchopneumonia. Arteriosclerosis. Heart: Some coronary sclerosis and brown atrophy.	144
39	Carcinoma of the transverse and sigmoid colon. Intestinal obstruction. Fecal fistula. Thrombophlebitis, right iliac vein. Pulmonary emboli. Septicemia. Heart: Some brown atrophy.	244
40	Malignant lymphoma, Hodgkin's type. Bronchopneumonia. Arteriosclerosis.	244
18	Carcinoma of the cervix. Gangrene of the pelvic organs. Hydronephrosis and hydroureter. Uremia. Generalized arteriosclerosis. Heart: Some brown atrophy.	251
17	Acute and chronic cholecystitis with stones. Cholecystoduodenal fistula, perforation of gallbladder. Acute intestinal obstruction. Acute gangrenous ileitis, generalized peritonitis. Diabetes mellitus. Generalized arteriosclerosis. Heart: Some brown atrophy and cloudy swelling.	262

Influence of Age.—The ages of the individuals in the normal group ranged from five months to sixty-nine years. Contrary to the findings in skeletal muscle, in which young individuals have lower creatine con-

tents, there is no apparent difference in cardiac creatine at different ages (Table III).

TABLE III

INFLUENCE OF AGE ON THE CREATINE CONTENT OF THE NORMAL HEART

AGE	NUMBER OF CASES	COMPARABLE CREATINE MG. PER CENT
Under 1 year	1	203
1- 9 inclusive	4	194
10-19 inclusive	none	
20-29 inclusive	6	177
30-39 inclusive	9	195
40-49 inclusive	6	195
50-59 inclusive	11	204
60-69 inclusive	11	192
Total	48	194

Decompensated Hearts

There were 17 cases that showed evidence of cardiac decompensation either clinically or at post-mortem examination. Some of these were frank insufficiencies, obviously the cause of death, while other cases were only mildly decompensated. This group is made up mostly of hypertensive hearts, rheumatic valvular hearts and nephritic hearts. There was one case of pernicious anemia with brown atrophy and resulting heart failure. There was one case of chronic adhesive pericarditis with failure. Table IV is a summary of the results found in this group.

TABLE IV

SEVENTEEN DECOMPENSATED HEARTS

	MEAN	STANDARD DEVIATION
Creatine, mg. per cent of moist weight	147	37
Water, per cent	79.47	0.87
Creatine, mg. per cent of dry weight	720	185
Comparable creatine, mg. per cent	144	37

In comparing these results with those found in the normal cases, it is seen that the creatine content of the decompensated hearts averages 50 mg. (25.8 per cent) lower than the normal. Statistically it is found that, according to Fisher's formula,[12] "t" is equal to 5.1. This indicates that the difference between the normal group and the decompensated group is highly significant.

It might be pointed out that of these 17 decompensated hearts, 6 fell within the normal range. The remaining 11, however, were definitely low, their values ranging from 92 to 152 mg. of creatine per 100 grams of tissue.

The question naturally arises whether the lower creatine content of the decompensated heart is due to an actual decrease in the creatine of the muscle fiber itself, or to other changes which might alter the relative

amount of muscular tissue in the myocardium. It is known that fibrous tissue contains much less creatine than muscular tissue. Scarring, therefore, lowers the creatine content of a muscular organ. Although great care was taken to avoid using portions which contained gross scar tissue, it is obviously impossible to exclude the microscopic "patchy areas of scarring" in hearts which contain it.

That the factor of increased fibrous tissue is negligible in this series, however, is shown by the fact that the hearts with scarring had a higher average creatine content (153 mg.) than those in which no increase of fibrous tissue was reported (136 mg.).

It is interesting to note that some of the lowest creatine values were obtained in decompensated hearts which, aside from hypertrophy, were without any obvious pathological change, either macroscopic or microscopic.

Miscellaneous Group

Fifteen cases are listed here which were not decompensated, but which could not be included in the normal series. They include cases with clinical manifestations of cardiac disease, pathological evidence of myocardial damage, hypertrophied hearts (compensated), etc.

SAMPLE NO.	DIAGNOSIS	COMPARABLE CREATINE, MG. PER CENT
31	Gas gangrene following perforating gunshot wound of chest. Profound shock. Sepsis. Myocardium shows extensive degenerative changes.	68
11	Tb. Nephritis. Auricular fibrillation.	144
32	Ruptured aortic aneurysm resulting in hemopericardium. Cardiac hypertrophy.	152
65	Diabetes. Chronic vascular nephritis. Terminal uremia. Hypertension. Cardiac hypertrophy. Acute streptococcic pericarditis. Some scarring of myocardium, some coronary sclerosis.	158
28	Renal carcinoma extending into renal vein, vena cava, and right auricle. Cause of death, neoplastic pulmonary embolus. Heart hypertrophied and dilated.	159
14	Osteomyelitis. Septicemia. Urinary infection with retention. Myocardium shows cloudy swelling, fragmentation, vacuolization.	159
34	Adenocarcinoma of sigmoid colon. Postoperative peritonitis. Septicemia. Adiposity of heart. (Muscle fibers separated by numerous strands of fat cells which extend nearly through the entire width of the myocardium.)	163
29	Empyema. Auricular fibrillation.	164
30	Old rheumatic valvular heart disease (compensated) with auricular fibrillation, cardiac hypertrophy and dilatation. Acute endocarditis. Septicemia. Septic emboli to vessels and spleen.	165
79	Chronic vascular nephritis with terminal uremia. Arteriosclerosis. Hypertension. Cardiac hypertrophy. Fibrinous pericarditis. Coronary sclerosis.	172

42	Bronchopneumonia following fracture of femur. Septicemia. Thrombophlebitis. Acute vegetative endocarditis. Slight cardiac enlargement.	173
35	Adenoma of thyroid. Septicemia. Thrombophlebitis. Infarcts of kidneys and spleen. Left cardiac enlargement. Auricular fibrillation. Hypertension.	174
60	Carcinoma of larynx, with laryngeal obstruction. Arteriosclerosis. Hypertrophy and dilatation of the heart. Some scarring of the myocardium.	189
41	Otitis media and mastoiditis with overwhelming septicemia; involvement of brain, kidneys, vessels, spleen, meninges, heart. Acute bacterial endocarditis, acute myocarditis, acute pericarditis.	195
72	Chronic vascular nephritis. Hypertension. Cardiac hypertrophy and dilatation. Acute parotitis. Acute pneumonia. Some myocardial scarring.	208

TABLE V

FIFTEEN MISCELLANEOUS HEARTS

	MEAN	STANDARD DEVIATION
Creatine, mg. per cent of moist weight	165	30
Water, per cent	79.68	0.65
Creatine, mg. per cent of dry weight	814	151
Comparable creatine, mg. per cent	163	30

Table V summarizes the results of the miscellaneous group.

It is evident that the creatine content of this group falls between the value found for the normals and that found for the decompensated hearts. This is shown graphically in Chart 1. That this group has a creatine value which is definitely lower than normal is shown by the fact that Fisher's "t" is equal to 3.1.

EFFECT OF SEPTICEMIA ON CREATINE CONTENT OF THE HEART

Denis[6] reported that septicemia is accompanied by a loss of creatine from the skeletal muscles. That such is apparently not the case in cardiac muscle is shown in Table VI.

TABLE VI

EFFECT OF SEPTICEMIA ON THE CREATINE CONTENT OF THE HEART

	SEPTICEMIA PRESENT		SEPTICEMIA ABSENT	
	NUMBER OF CASES	COMPARABLE CREATINE, MG. PER CENT	NUMBER OF CASES	COMPARABLE CREATINE, MG. PER CENT
Normal group	34	193	14	197
Decompensated group	9	145	8	143
Miscellaneous group	9	164	6	161

EFFECT OF HYPERTROPHY PER SE ON THE CREATINE CONTENT

In the decompensated series, all but three hearts were hypertrophied. These three averaged 149 mg. of comparable creatine per 100 grams of tissue, which is not significantly different from the average for this series.

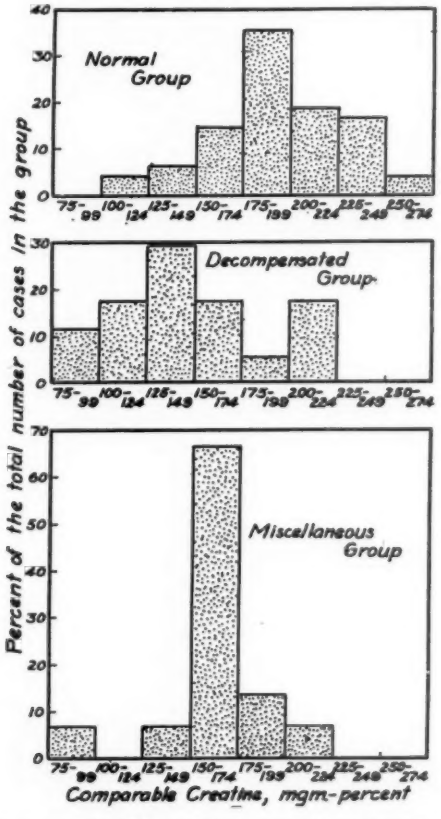

Chart 1.—Comparison of comparable creatine content of normal, decompensated, and miscellaneous hearts.

In the miscellaneous series the results are as listed in Table VII. The difference between the means in this comparison is 23. The value of "t" in Fisher's formula is 1.5, which is too low to show much significance; it indicates that there is a possibility that the hypertrophied hearts have a higher creatine content as compared with nonhypertrophied hearts.

TABLE VII

EFFECT OF HYPERTROPHY ON THE CREATINE CONTENT OF THE HEART (MISCELLANEOUS GROUP)

	NUMBER OF CASES	COMPARABLE CREATINE, MG. PER CENT
Hypertrophied	9	172
Not hypertrophied	6	149

SUMMARY

The left ventricular myocardium of 48 approximately normal human hearts had an average creatine content of 194 mg. per 100 grams of tissue, this value being based upon an arbitrary water content of 80 per cent.

There were neither sex nor age differences in this creatine content.

A few cases included in the normal group, but having creatine contents differing widely from the mean, are listed separately with diagnoses given in detail.

Analyses of 17 decompensated hearts showed a significantly lower average creatine content than normal. Scar tissue was not a significant factor in producing this low value.

Fifteen abnormal, but not decompensated, hearts had an average creatine content significantly lower than normal, but higher than the values for the decompensated hearts. These are listed separately, with their diagnoses given in detail.

Septicemia per se had no effect upon the creatine content of the left ventricle.

An effect of hypertrophy per se on the creatine content of the heart was not definitely established.

These findings suggest that the "reserve" of the heart closely parallels its creatine content.

I am indebted to the Staff of the Pathology Department for making the post-mortem material and the records available.

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DIABETES AND CORONARY THROMBOSIS*

An Analysis of Cases Which Came to Necropsy

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MANY reports dealing with the vascular complications of diabetes have recently been published. Of the 1,784 deaths of diabetic individuals in New York City in 1930,[1] more than half were due to cardiovascular-renal disease. Particular emphasis has been laid upon the frequent association of diabetes and coronary disease. In his excellent monograph, Levine[2] states that diabetes has a most important bearing on the development of coronary thrombosis.

Because abundant clinical and post-mortem material was available, it was decided to review our records and compare results with those of other observers. Only cases which came to necropsy were studied.

GROUP I

Ninety-two cases of diabetes were analyzed as to age, sex, and coronary artery pathology. The latter was divided into thrombosis with infarction, thrombosis alone, and slight, moderate and marked sclerosis. The results are shown in Table I.

Table I

AGE	THROMBOSIS WITH INFARCT	THROMBOSIS ALONE	CORONARY SCLEROSIS			NEGATIVE	TOTAL
			SLIGHT	MODERATE	MARKED		
10-19						1	1
20-29						1	1
30-39						3	3
40-49	1		2	3		5	11
50-59	8		3	6	7	4	28
60-69	8	4	7	7	7	2	35
70-79	5			2	5	1	13
Total	22	4	12	18	19	17	92

There were 26 cases of thrombosis with or without infarction (28 per cent). Twenty of the 26 occurred in the 50-69 year age group. The average age of these 20 was 61 years. Thirteen were male and 7 female.

There were 16 cases under the age of 50 years. Only one of these showed occlusion; 10 showed no pathological changes in the coronary arteries.

*From the Medical Division of Montefiore Hospital, New York City.

The average age of the entire group was 58.5 years. The average duration of the diabetes was 7 years.

There were 19 patients with gangrene of the extremities, all over the age of 50 years. Nine had occlusion and 6 marked sclerosis of the coronary vessels. This would tend to confirm the clinical impression that cases with gangrene are very likely to have severe coronary disease.

GROUP II

For the purpose of comparing age and sex a group of 96 nondiabetic cases with the pathological diagnosis of coronary artery disease was then studied. The results are shown in Table II.

TABLE II

AGE	THROMBOSIS WITH INFARCT	THROMBOSIS ALONE	CORONARY SCLEROSIS			TOTAL
			SLIGHT	MODERATE	MARKED	
20-29		1				1
30-39				1		1
40-49	4	3	2	1	2	12
50-59	15	2		2	4	23
60-69	34	4		2	7	47
70-79	6	1		1	2	10
80-		1			1	2
Total	59	12	2	7	16	96

Of the 71 cases of thrombosis with or without infarction, 55 occurred in the 50-69 year age group. The average age of these 55 was 61 years; ten were female.

The average age of the entire group was 60 years.

Both groups are compared in Table III.

TABLE III

		DIABETIC	NONDIABETIC
	Total number cases	92	96
	Average age	58.5	60
	Number with occlusion	26	71
50-69 Years	Number of cases	63	70
	Number with occlusion	20	55
	Average age (occlusion)	61	61
	Males (occlusion)	13	45
	Females (occlusion)	7	10
	Per cent females	35	18

It is evident that the majority of all our cases occurred between the ages of 50 and 69 years. Here, too, were found the greatest number with occlusion.

The average age of both groups was about the same, and was exactly the same in the cases of occlusion occurring in the 50-69 year age group.

Occlusion occurred more frequently in diabetic than in nondiabetic females (35 to 18 per cent).

GROUP III

One hundred diabetics past the age of 40 years were studied to determine the extent of vascular changes in heart, kidneys, aorta and extremities. Results are shown in Table IV.

TABLE IV

	CASES
Coronary occlusion	34
Coronary sclerosis	45
Atherosclerosis of aorta	79
Arteriosclerosis and arteriolosclerosis of kidneys	70
Gangrene of extremities	19
Hypertension	44

Levine[2] found that 34, or 23.7 per cent, of a total of 145 cases of coronary occlusion had diabetes or glycosuria. Twelve of the 34 were females (35 per cent). Of the remaining 111 nondiabetics, 22 were females (about 20 per cent). Here our figures agree quite closely. The average age of his diabetics was 58.1 years, and for the entire group it was 57.8 years.

Warren[3] examined the hearts of 282 diabetic cases and found 34 cases of thrombosis with infarction. Nine were fresh, 18 healed and 7 fresh and healed. For the 18 cases of healed infarcts, the average duration of the diabetes was 12.5 years and the average age 63.7 years.

Gibb and Logan[4] in reviewing 147 diabetic autopsies found myocardial infarction in only 11 cases, all in patients over the age of 40 years.

Among 55 autopsied diabetics Root[5] found coronary sclerosis in 33 cases.

Wilder[6] examined the hearts of 49 diabetic patients who came to post-mortem examination and found that 17, or 34 per cent, showed coronary sclerosis.

Of 77 necropsies on diabetic patients, Blotner[7] reports that 35, or 45 per cent, showed abnormal coronary vessels. Coronary thrombosis occurred in 8, or 23 per cent, of the 35 cases. Twenty-eight of the 35 cases were in the sixth, seventh and eighth decades.

Warren and Root[8] report their findings in 26 autopsied cases of diabetes. Ten, all over the age of 48 years, had coronary sclerosis. Of 17 patients over 40 years, 4 had myocardial infarcts and 5 extreme sclerosis of the coronary vessels.

Nathanson[9] reviews 100 necropsies of patients who had suffered from diabetes. Of 26 below the age of 50 years only 2 show coronary disease. Of 74 cases over 50 years, 39, or 52 per cent, show coronary involvement.

GROUP IV

To determine the relative frequency with which coronary occlusion occurs in diabetics and nondiabetics, we reviewed 594 consecutive autopsied cases whose ages ranged between 50 and 69 years. The results are shown in Table V.

TABLE V

	DIABETIC	NONDIABETIC
Number of cases	74	520
Number with coronary occlusion	23	77
Percentage with coronary occlusion	31	16

Of 100 cases with coronary occlusion, 23 were diabetic. This compares favorably with Levine's[2] 23.7 per cent. The incidence of occlusion was twice as great in our diabetic group. We fully recognize the dangers of comparing so small a group with the much larger nondiabetic group. However, we feel quite certain that coronary occlusion is more common in diabetics. Blotner[7] reports an incidence of 45 per cent in diabetics as compared with 21 per cent in nondiabetics above the age of 40 years. His findings relate only to coronary sclerosis. Nathanson[9] gives the following figures for individuals past the age of 50 years: coronary disease in diabetics 52 per cent; in nondiabetics 8 per cent.

The greater incidence of coronary disease in diabetic as compared with that in nondiabetic women may be explained partly by the more frequent occurrence of diabetes in females. Wendt and Peck[10] studied 1,073 cases of diabetes and found among them twice as many females as males. This was particularly true of the group between 40 and 60 years.

DISCUSSION

Even if it is granted that the older diabetic patient presents the picture of extensive vascular degeneration, it does not at all follow that diabetes is an etiological factor in the production of atherosclerosis. Indeed, one might offer this as proof, with equal justification, that diabetes is a manifestation of atherosclerosis. The introduction of insulin has caused us to alter many ancient concepts concerning diabetes. Yet the dogma that the abnormal metabolism found in diabetic individuals favors or hastens the production of atherosclerosis is as widely adhered to as ever. When one examines the scanty evidence upon which this belief is founded, one cannot help but marvel at the universal acceptance accorded this view.

Joslin[11] has championed the Aschoff modification of Virchow's imbibition theory of arteriosclerosis. It is believed that there is a fatty deposition in the wall at the site where vessels are under physiological strain. The fats are derived from the greater concentration of lipoids,

especially cholesterol esters, in the plasma. Joslin[12] states that the evidence implies that the increasing incidence of arteriosclerosis in the diabetic individual can be checked and the earlier types of arteriosclerosis can be overcome by a diet which provides for the complete oxidation of fat. In a recent paper by Joslin[13] it is most interesting to read that "one would like to say that arteriosclerosis could be avoided or at least postponed if the cholesterol in the blood as a representative of all the lipids could be kept normal; and this may be true, but the evidence is insufficient."

Moscheowitz[14] believes that arteriosclerosis is due to circulatory stress such as is caused by hypertension. He states that an increasing doubt has arisen as to whether experimental cholesterol arteriosclerosis represents human arteriosclerosis.

Despite the fact that excess of cholesterol of the blood is an exception in uncomplicated diabetes in children,[15] attempts have been made to establish the presence of premature arteriosclerosis in the young diabetic patient. Since death in the latter is a rarity, investigators have had to resort to radiographic methods to demonstrate calcification of the vessels of the lower extremities. Morrison and Bogan[16] reporting from Joslin's clinic found that 53 per cent of 324 diabetic patients showed calcification of the vessels of the lower extremities. Critical analysis of their tables reveals, however, that of 121 cases under the age of 40 years, only 5 are positive. There are 25 patients under the age of 40 years who have had diabetes for 5 years or longer, and only 3 of these show calcified vessels. Calcification was most marked in the fifth to the eighth decades.

Reporting also from Joslin's clinic, Shepardson[17] examined 50 cases of patients under the age of 40 years who had had diabetes for 5 years or more. Eighteen, or 36 per cent, showed radiographic evidence of calcified vessels, an astonishingly high figure. We find it difficult to reconcile her results with those of Morrison and Bogan, particularly as both report from the same clinic.

White and Hunt[15] found that 9 of 48 diabetic children had x-ray evidence of arteriosclerosis.

Bowen and Koenig[18] report on 58 cases in which the diabetes had been unprotected with insulin for less than 5 years. Seventeen showed calcification of the vessels of the feet. Fourteen of these 17 occurred in the sixth, seventh and eighth decades. Of their 58 cases there were 20 under the age of 40 years, and but one of these showed calcification.

From the above it can be seen that advocates of the premature arteriosclerosis theory cannot agree among themselves. In addition there is lacking adequate data on the vessels of normal controls under the age of 40 years. If arteriosclerosis be present to the extent that some would have us believe, why is not gangrene seen in the young diabetic patient?

Valuable information can be obtained from examining the eyegrounds of diabetic patients. The retinitis found in diabetes is the retinitis of arteriosclerosis.[19] Of 44 patients with retinal disease reported by Wagener and Wilder[20] all but two were more than 40 years old. Of these two, one had nephritis and the other hyperemia of the optic nerve which probably had no connection with the diabetes.

Spalding and Curtis[21] investigated 307 cases of diabetes and found that 207, or 67 per cent, had no abnormalities of the retina. Included in these are 17 children under 16 years of age. Forty-six, or 15 per cent, showed retinal arteriosclerosis with no other changes; 16, or 5 per cent, had retinitis, all showing arteriosclerosis of the retinal vessels as well. Ten of the 16 had peripheral arteriosclerosis also. Hypertension was a consistent finding in cases with retinal arteriosclerosis and retinitis. The authors regard the retinitis found in diabetes as that of hypertensive cardiovascular disease. Of their 16 cases with retinitis, 75 per cent had hypertension and impaired renal function. If diabetes causes premature atherosclerosis, why is not retinitis seen in the young diabetic patient?

One is likely to lose sight of the frequency with which hypertension occurs in the older diabetic. Forty-four of one hundred cases past the age of 40 years had hypertension. When one considers that there were 34 cases of coronary occlusion in the hundred, one can well suspect that the incidence of hypertension was at one time much greater. Fishberg[22] calls attention to the fact that the older diabetic patient is very liable to have essential hypertension. The same author comments that in some cases of essential hypertension with diabetes it is possible that pancreatic arteriolosclerosis, due to the hypertension, is responsible for the disturbance in carbohydrate metabolism. Joslin[23] found that 33 per cent of his older diabetic patients had hypertension. Kramer[24] found hypertension in 39 per cent of 500 diabetics. He attributes both hypertension and diabetes to a common cause. He states that a pre-existing hypertension produces changes in the vessels of the pancreas and this in turn reacts upon the activity of the islands of Langerhans. Major[25] found the systolic blood pressure of elderly diabetic patients higher than that of normal controls. That hypertension is an important factor in the production of coronary disease is generally admitted. Levine[2] ranks it first as an etiological cause. Fishberg[22] states that the large majority with essential hypertension develop arteriosclerotic changes of the coronary arteries.

If hypertension is so important in the production of coronary atherosclerosis and if hypertension is so frequently encountered in the older diabetic, why is it necessary to invoke diabetes as a causative factor?

The pancreas is frequently involved in arteriosclerosis. In describing the distribution of arteriolosclerotic lesions Fishberg[22] lists the kidney first and the spleen, pancreas, liver and brain next in the order of

frequency of occurrence. Discussing the nature of the disease, he regards the changes in the arterioles as a manifestation of the wear and tear to which they have been subjected.

Barron[26] made careful post-mortem studies of the pancreas in cases of coronary sclerosis and found advanced atherosclerosis of the pancreatic arteries. He believes pancreatic atherosclerosis to be a relatively common condition associated with cases of advanced hypertension and with coronary sclerosis. The diabetes in these cases is probably due almost entirely to this lesion.

Eighteen of Warren and Root's[8] 26 autopsied diabetic cases showed arteriosclerosis of the pancreatic vessels.

Evidence of vascular involvement of other organs is frequently found in the aged diabetic patient. Of our hundred cases past the age of 40 years, 79 had generalized atherosclerosis; 70 had arterio- and arteriolosclerosis of the kidneys; 19 had gangrene of the extremities; and 11 had cerebral arteriosclerosis. Joslin[27] calls attention to the occurrence of peptic ulcer in 30 of his cases. Jankelson and Rudy[28] report 6 cases of diabetes with ulcer. All but one were in patients over 50 years old. Ophüls[29] has described the relation of peptic ulcer to arteriosclerosis. He says, "In studying arteriosclerosis the rather common occurrence of gastric or duodenal ulcer in arteriosclerotics became so evident that almost unconsciously I began to look on it as a lesion comparable to arteriosclerotic scars in heart and kidney." To which we add, "and pancreas."

If diabetes be related to coronary disease, the latter should be found quite commonly in the young diabetic patient, for it is here that the metabolic disorder is most severe. Before insulin days these young people died too soon after the onset of their symptoms to permit the development of pathological changes in other organs. It is now ten years since the introduction of insulin, and the young diabetic patient continues to live and thrive. During this period a fairly large number should have died of coronary disease. Only a few such cases have been described. Warren[3] reports a patient who had diabetes for eight years and died at the age of thirty-three years of coronary disease. He also mentions a personal communication relating to a diabetic patient who died at twenty-two years of coronary thrombosis.

Coronary thrombosis may occur in young nondiabetic persons. Smith and Bartels[30] report two cases of coronary thrombosis in nondiabetic persons aged thirty-five and thirty-six years. They review 21 cases previously reported, all under the age of 40 years, with ages ranging from 12 to 39 years. Sutton and Brandes,[31] reviewing 340 nondiabetic cases which came to necropsy and in which gross coronary sclerosis was found, comment on the early age at which definite arteriosclerotic changes were disclosed. The youngest was 5 years old, and in a boy of 12 years definite gross sclerosis of the large coronary arteries was

evident. They found 42 cases of coronary sclerosis in the second, third and fourth decades. We attach great significance to the fact that the young diabetic person has done so splendidly, for it is perhaps the best proof that he has not developed atherosclerosis prematurely.

Warren[3] calls attention to the long duration of the diabetes before the onset of coronary symptoms. He states that proof that the diabetes is not merely an incidental feature in these cases is to be found in the diabetic process long antedating the cardiac condition. Several objections to this are obvious. Urinalysis is part of a routine physical examination; an electrocardiogram is not. Coronary disease may be present for a long period and yet give no signs or symptoms until myocardial ischemia develops. Even under these circumstances the electrocardiogram (as interpreted in the past) may reveal nothing. Diabetes lends itself much more readily to detection than does coronary disease.

Based on his material, Leutenegger[32] states that he cannot demonstrate that there exists a special diabetic arteritis characterized by frequency or prematurity. In his cases the vascular changes clinically occur in the sixth and seventh decades, in the same age group in which vascular changes are most common in the nondiabetic person as well.

Gray and Sansum[35] note a low incidence of arteriosclerosis in their series before the fifth decade, even in cases where the diabetes is of long duration. They find arteriosclerosis to be more closely related to the age of the patient than to the duration of the diabetes.

Nathanson[9] believes that at the present time it does not seem justifiable to conclude that diabetes is a causative factor in the production of arteriosclerosis, as no mechanism for this process has been satisfactorily proved.

Cruickshank[33] states that it is considered more probable that these two conditions result from a common cause (vascular degeneration) than that the glucosuria is an etiological factor in the production of coronary thrombosis.

John[34] regards the diabetes occurring in middle age as comparable to the failure of other functions in the body resulting in heart and kidney disease and hypertension. The effect of age upon carbohydrate tolerance is well known. In this connection, the work of Marshall[36] is worthy of mention. This investigator studied glucose tolerance in a series of men whose average age was 72 years. In a group of healthy old men he found that 14 per cent had normal blood sugar curves and 14 per cent had typical diabetic curves. In a group of "unhealthy" subjects suffering from chronic bronchitis, arthritis, cancer, etc., he found that 14 per cent had normal curves and 50 per cent had diabetic curves. The others had atypical sugar tolerance curves. He also studied 5 individuals who were grossly senile and found that 3 of these had diabetic curves. Commenting on the high incidence of diabetic

curves, he states that this can be regarded as indicative of the marked disturbance of the carbohydrate mechanism which may occur in a certain proportion of aged people.

We prefer to regard diabetes in people past the age of 40 years as a manifestation of degenerative vascular disease. By so doing, we very properly minimize the metabolic disorder and stress the condition of the vascular tree. If diabetes of middle age is interpreted as clinical evidence of generalized arteriosclerosis, it is reasonable to expect that a large number of diabetic patients will also have coronary artery disease.

SUMMARY

1. Twenty-six of 92 diabetic patients showed coronary thrombosis. Twenty cases of coronary artery thrombosis occurred in the sixth and seventh decades.

2. Coronary thrombosis occurred more frequently in the diabetic than in the nondiabetic female patient.

3. In both diabetic and nondiabetic patients coronary thrombosis occurred predominantly in the sixth and seventh decades.

4. Of 100 diabetic patients past the age of 40 years, 34 showed coronary thrombosis and 45 coronary sclerosis. Seventy-nine had atherosclerosis of the aorta. Seventy showed arteriosclerosis and arteriolosclerosis of the kidneys. Nineteen had gangrene of the lower extremities. Hypertension was present in 44 cases.

5. Coronary thrombosis occurred twice as frequently in diabetic as in nondiabetic patients.

6. The opinion is expressed that both coronary thrombosis and diabetes in individuals over the age of 40 years are manifestations of degenerative vascular disease.

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THE BLOOD PRESSURE OF CHINESE LIVING IN EASTERN CANADA*

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A STUDY of blood pressure in groups of people of different races and nationalities is of importance in setting standards of normal averages among them. It also serves to reveal the incidence of hypertension as well as the influence of such factors as environment, mode of living and heredity on the height of systolic and diastolic blood pressure. Arterial hypertension—so common in civilized countries, particularly in the temperate zone—is of quite infrequent occurrence in China (Cadbury,[1] Cruickshank,[2] Kilborn,[3] Foster[4]). It is generally recognized, too, that the blood pressure of Chinese living in China is at a lower level than the accepted standards for Americans and Europeans. Reports in the literature show that this is true for different sections of that densely populated country.

LITERATURE

Cadbury[1] found in a series of healthy Cantonese (South China) students that the systolic pressure averages 20-30 mm. Hg less and the diastolic 10-20 mm. lower than the standards for European and American men of corresponding age, weight and height. The analysis of the records of natives living in Northern China by Tung,[5] showed a mean systolic of 102 mm. for the ages fifteen to nineteen years, and 113 mm. for fifty to fifty-four years, with a corresponding rise in the diastolic from 64 to 73 for the same age periods. Kilborn[3] examined 700 Szechwanese (West China) students and obtained a mean systolic pressure of 111 mm. and diastolic of 70 mm. Similarly, Ying[6] in a report of a smaller group living in Chekiang (East Central China) obtained average figures of 110-118 with a rise above 125 mm. for groups over fifty years of age. In contrast to these studies are the observations of Alvarez,[7] who in 6,000 healthy American men ranging in age from sixteen to forty years found an average systolic blood pressure of 129 mm.

It is generally accepted that the pressure of normal adults of Anglo Saxon origin is about 120-125 mm. and diastolic 80-85 mm. (Symonds,[8] Woley[9]), although somewhat higher readings are still considered normal. Thus Hunter and Frost's[10] statistics show that the average normal systolic pressure varies from 120 to 135 and diastolic from 80 to 89 for the ages twenty to sixty years. In contrasting blood pressures of Chinese

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and Americans, the evidence therefore seems to show that the former's level is consistently about 10-15 mm. lower than that of the latter. Another interesting fact is revealed in the influence of environment on the height of blood pressure. Tung[11] recorded the pressure of 30 Chinese students in America and again in Peking three years later. An average drop of 11 mm. in systolic and 8 mm. in diastolic was noted after their return to China. In 58 Americans studied in the same way, this author[12] showed that a distinct decrease in blood pressure occurs in Westerners residing in China. Foster[4] came to the same conclusion, for in a group of 120 Americans living in Hunan, he found that the average pressure approached that of the local Chinese population. With these observations in mind, it seemed of interest to investigate a group of Chinese living in Canada in order to determine their average blood pressure. Such a study would also indicate the frequency of arterial hypertension among them.

PROCEDURE

Two hundred and thirty-nine Chinese living in the city of Montreal, whose ages range from seven to sixty-nine years (Table I) form the basis of this report. Only 4 females are included because of the small number of Chinese women in the local colony. Practically all Chinese in this community came originally from Canton and the immediate neighborhood in the south of China. The majority have lived here for many years with only occasional brief visits to China. Many of them have become thoroughly acclimatized to our Western civilization. Their occupations (Table II) are for the most part manual labor in laundry or kitchen.

TABLE I

AGE DISTRIBUTION OF 239 CANADIAN CHINESE

AGES	NUMBER OF SUBJECTS
5–9 years	3
10–19	8
20–29	31
30–39	50
40–49	81
50–59	54
60–69	12

Most of the blood pressure records were taken during the week-ends, when the Chinese assemble for diversion and amusement. All readings were done by the author and in the mid-afternoon or early evening. A standard mercury sphygmomanometer was used with a 12 cm. cuff. The beginning of the first and fourth phases was regarded as systolic and diastolic pressure respectively. The subjects sat comfortably in a chair, resting one arm on an adjoining table. With a few exceptions, they had not worked immediately before the recording of the pressure. The Chinese are rather phlegmatic and on that account did not manifest un-

due nervousness at the procedure. In each case information was elicited relating to the duration of residence in Canada, the number of visits to China, age, height, weight and occupation. The heights and weights are necessarily approximate because there was no opportunity to corroborate

TABLE II

OCCUPATIONS OF 239 CANADIAN CHINESE

Laundry worker	–	101	(42.2%)
Cook	–	35	
Merchant	–	30	
Restaurant owner	–	22	
Student	–	11	
Housewife	–	3	
Waiter	–	2	
Teacher	–	2	
Taxi driver	–	2	
Physician	–	1	
Tailor	–	1	
Barber	–	1	
Engineer	–	1	
Clerk	–	1	
Unemployed	–	16	
Not recorded	–	10	
Total	–	239	

these measurements. When the first blood pressure reading was found to be 140 mm. (systolic) or over, the subject was instructed to rest quietly while sitting in the chair and the reading repeated after five minutes. The blood pressure was checked in these instances because of the well-known tendency of nervousness and excitement to cause a rise in systolic pressure. In several instances three consecutive readings were made in the same subject. In a number of normal individuals, and particularly in those with hypertension, the heart was examined for evidence of valvular disease and enlargement. The pulse rate and presence or absence of peripheral arteriosclerosis were noted as frequently as possible.

OBSERVATIONS

Blood Pressure and Duration of Residence in Canada.—The majority of the Chinese in Montreal have been living here for ten years or longer; therefore one cannot correlate the height of the blood pressure with the length of time they have been residing here. Thus only 4 subjects have been in this country less than five years, and 8 between six and nine years. Ninety-one have been residents of Canada for from ten to nineteen years and 116 have been here for more than twenty years. The average for all cases, excluding those born in Canada, is nineteen and one-half years. It may be mentioned, however, that the more recent immigrants do show a distinct tendency toward hypotension. Thus a male, aged forty-three years, in Canada three years, has a blood pressure

of 78/58; another, aged thirty-six years, in Canada four years, has a bloood pressure of 102/66; and a third, a young Chinese physician aged twenty-five years, in Canada also for four years, was observed to have a pressure of 104/84.

TABLE III

RELATION OF BLOOD PRESSURE TO HEIGHT AND WEIGHT IN 20 CANADIAN-BORN CHINESE

SEX	AGE (YR.)	HEIGHT (CM.)	WEIGHT (KILOS)	BLOOD PRESSURE SYST. & DIAST.
Male	10	111.7	30.4	104 : 76
Male	24	162.5	60.0	126 : 80
Male	7	----	20.4	110 : 84
Male	10	----	32.2	116 : 74
Male	9	----	25.0	112 : 78
Female	31	154.9	60.0	112 : 78
Female	7	99.0	20.0	98 : 66
Female	20	160.0	50.0	122 : 74
Male	33	167.7	74.5	120 : 94
Male	16	167.7	52.2	128 : 79
Male	22	171.4	55.9	116 : 78
Male	22	171.4	56.3	125 : 82
Male	23	175.3	61.8	116 : 88
Male	28	165.1	61.3	116 : 86
Male	18	170.2	84.0 (obese)	124 : 86
Male	14	152.4	35.9	112 : 78
Male	18	162.5	----	124 : 92
Male	17	170.2	55.0	122 : 78
Male	34	162.5	59.0	116 : 74
Male	14	152.4	60.00 (overweight)	124 : 96
		Average systolic = 117.1 mm.		
		Average diastolic = 81.0 mm.		

Blood Pressure in Canadian-Born Chinese.—Twenty individuals are included in this category, and Table III shows the relation of their blood pressure to height and weight. All have normal pressures, and when averaged the systolic equals 117.1 mm. and the diastolic 81.0 mm. When we compare these figures with those reported in native Chinese of similar age periods, we find that the Canadian subjects have definitely higher systolic and diastolic pressures. The average blood pressure in this latter group is lower than that obtained for the series of 239 cases, but the two are not comparable because the Canadian-born subjects number only 20 in all and are predominantly in the younger age periods of life.

The Average Blood Pressure for Different Ages.—A comparison of the mean or average blood pressure obtained in our group with that reported by Ying[6] for similar age periods is shown in Table IV. It is obvious that the average systolic pressure of Chinese living in Canada is distinctly higher (by about 10 mm.) for each decade than that for natives living in China, especially in young and middle-aged adults. In both a slight but steady increase in pressure occurs with advancing age and in the later decades (fifty to sixty-nine years) there is a sharp rise which almost reaches 140 mm. In our subjects this may be accounted for by the greater frequency of hypertension in the older men.

TABLE IV

COMPARISON OF AVERAGE BLOOD PRESSURE FOR DIFFERENT AGES IN CANADIAN CHINESE (239) AND IN Y. Y. YING'S CHEKIANG NATIVES (259)

AGE	NUMBER		AVERAGE SYST.		AVERAGE DIAST.		MAXIMUM SYST.		MAXIMUM DIAST.		MINIMUM SYST.		MINIMUM DIAST.	
	AUTHOR	YING	AUTHOR	YING	AUTHOR	YING	AUTHOR	YING	AUTHOR	YING	AUTHOR	YING	AUTHOR	YING
5- 9	3	22	106.6	96.3	76.0	64.8	112	110	84	75	98	80	66	55
10-19	8	116	119.2	107.0	82.3	71.0	128	135	96	95	104	80	74	50
20-29	31	58	121.4	111.6	82.7	71.3	145	130	100	90	104	90	68	50
30-39	50	29	123.9	112.4	82.3	71.7	170	135	110	90	102	90	44	50
40-49	81	18	124.0	118.3	82.0	75.6	204	140	116	100	78	95	56	60
50-59	54	12	138.6	126.8	88.2	76.6	215	140	132	90	90	110	48	65
60-69	12	4	137.7	136.2	87.8	73.7	165	140	104	90	112	125	66	55
			124.4	114.5	83.0	72.0								
			Average of total cases											

Thus for the ages fifty to sixty-nine years, 21 subjects had systolic pressures above 140 mm., whereas in the earlier decades there were only 14 above this level. This is even more striking when we bear in mind the fact that the 21 cases with hypertension occurred in a total of 66 subjects while the 14 younger hypertensives were found in 173 subjects. The average pressure in Canadian Chinese is in fact the same as that for white people of similar ages, living on this continent (Alvarez,[7] Symonds,[8] Woley[9]). The same conclusions hold true for the averages of diastolic pressure, though there is not such a significant rise with advancing age. Table IV shows that the average diastolic pressures of Canadian Chinese are higher than those of their compatriots residing in China.

TABLE V

RELATION OF SYSTOLIC BLOOD PRESSURE TO AGE IN 239 CHINESE

PRESSURE IN MM.	AGE IN YEARS							
	5-9	10-19	20-29	30-39	40-49	50-59	60-69	TOTAL
70- 79					1			1
80- 89					1			1
90- 99	1				2	1		4
100-109		1	4	8	10	1		24
110-119	2	2	9	13	13	8	1	48
120-129		5	12	12	28	11	3	71
130-139			5	12	18	16	4	55
140-149			1	2	3	6	1	13
150-159				2	1	1	1	5
160-169					3	3	2	8
170-179				1		3		4
180-189								0
190-199						2		2
200-209					1	1		2
210-219						1		1
Total	3	8	31	50	81	54	12	239

Relation of Systolic and Diastolic Blood Pressure to Age.—The levels of systolic and diastolic blood pressure for each decade are shown in Tables V and VI respectively. The majority of our cases (185 or 77.4 per cent) are in the age group between thirty and fifty-nine years. One hundred and seventy-four subjects (72.8 per cent) have systolic blood pressures ranging between 110 and 139 mm., whereas in 35 (14.6 per cent) the reading is above 140 mm. The largest single group of 71 cases occurs in the 120-129 mm. division. It is seen how few cases actually have pressures below 110 mm., thus explaining the higher mean pressure of Western Chinese as compared to those living in China. In the distribution of the diastolic records, 166 subjects (70.0 per cent) have readings below 90 mm., of which 76 have a pressure of 80-89 mm. In 20 (8.4 per cent) a pathological reading of over 100 mm. was found. Here, too, really low figures are relatively uncommon in the diastolic pressures of Canadian Chinese.

TABLE VI

RELATION OF DIASTOLIC BLOOD PRESSURE TO AGE*

PRESSURE IN MM.	AGE IN YEARS							
	5-9	10-19	20-29	30-39	40-49	50-59	60-69	TOTAL
40- 49				1		1		2
50- 59					2			2
60- 69	1		1	6	6	1	1	16
70- 79	1	5	9	21	23	10	1	70
80- 89	1	1	16	5	27	21	5	76
90- 99		2	4	12	16	14	3	51
100-109			1	3	3	2	2	11
110-119				2	2	4		8
120-129								0
130-139						1		1
Total	3	8	31	50	79	54	12	237

*In 2 subjects diastolic pressure could not be recorded, the sound disappearing shortly after the onset of the first (systolic) phase.

Blood Pressure and Obesity.—In a study of this kind, it is difficult to define precisely where obesity begins. It is generally agreed, however, (McLester,[13] Harrop[14]) that an excess of 25 per cent or more above the standard or ideal weight for age and height is to be considered abnormal. But many persons are found who are 20 pounds (9.0 kilos) or more above their ideal weight and these fall into the overweight class. Of our 239 Chinese, 11 were observed to be distinctly obese, and 12 were included in the second group of overweight individuals, giving a total of 23 or 10 per cent in the obesity group. In common with white people, the later decades are subject to obesity; thus 8 of the obese Chinese were in the fourth decade of life, 3 in the fifth and 9 in the sixth decade. When we come to examine the blood pressures of these, we find that 5 obese subjects have arterial hypertension; i.e., a systolic blood pressure above 140 mm., and 6 have diastolic pressures over 100 mm. There is therefore in this small group of overweight Chinese a higher incidence of hypertension (21.7 per cent) than in those of normal or average weight (10.1 per cent). This is in agreement with what is generally found, viz., that high blood pressures occur with greater frequency in those who are obese than in those who are not (Alvarez and Stanley,[7] Symonds,[8] Hartman and Ghrist[15]). It should be added that the diet of Canadian Chinese is a liberal one and moderately well balanced. In China the natives subsist largely on a vegetable diet.

Hypertension in Chinese.—A systolic pressure of 140 mm. Hg is usually regarded with suspicion at any age, and in the present study 2 consecutive readings above this level are held to be pathological and the cases included in the hypertensive group. There were 27 subjects (11.2 per cent) with such elevated pressures. It is quite possible that a number of these ought not to be considered hypertensive in view of the well-known effect of nervousness and apprehension in producing a rise of systolic pressure. And though most of the Chinese did not mani-

fest any uneasiness, yet the procedure of taking blood pressure was a strange one to many. As mentioned before, a five-minute rest interval was allowed between the first and second reading to remove as much of the nervous factor as possible. A number had undoubted hypertension with the systolic just below or above 200 mm., and in 13 subjects the diastolic was over 100 mm. In 14 cases the heart was examined, and in 6 of these there was confirmatory evidence of hypertensive disease manifested by cardiac enlargement and accentuation of the second aortic sound at the base. In one subject there was a mitral insufficiency with enlarged heart and in another pronounced peripheral arteriosclerosis. In 7 no evidence of organic or valvular heart disease could be elicited by ordinary physical examination. The heart was also examined in 25 subjects whose blood pressures were within normal limits, and in 2 cases rheumatic valvular heart disease was detected. The remainder were healthy.

The frequency of hypertension in Chinese living in Canada is certainly in marked contrast to its rarity in Chinese natives. Foster[16] states that among 4,000 Chinese admissions to the medical service of the Hunan-Yale Hospital in China, he was able to find less than 20 with a blood pressure of 160 or over. In his private practice in New England, however, 16 per cent of his office patients had pressures of 150 mm. or over.

The etiology of arterial hypertension remains obscure and several factors have been mentioned as contributory agents. Thus constitution, endocrine gland changes, diet, climate and mode of living have all been suggested as causes. Of these environment and mode of living deserve attention. In China, the tempo of life is certainly at a slower pace, and nervous strain, so characteristic of Western civilization, is relatively absent. Hypertension is rare among the natives, and even white people after a short residence are found to have lowered blood pressures. On the other hand, when the Chinese emigrate to this country, their blood pressures increase so that their average pressure is the same as that of the white inhabitants and hypertension is found frequently enough.

COMMENT

This work was undertaken to determine the blood pressure of Chinese living in Canada for a number of years and to compare their average pressure with that of the white inhabitants. The great majority of the subjects have been in Canada for ten years or more, and their average blood pressure is 10 mm. or more higher than that of Chinese natives for each decade. As a matter of fact, their pressures are equal to those reported for native Westerners. The astonishing finding of hypertension in 11 per cent of our subjects compared to its rarity in China, suggests the importance of the rôle of worry and

nervous strain of western life, as well as dietary and other environmental factors, in the etiology of high blood pressure. In a small number of Canadian-born Chinese the average pressure was observed to be well above that reported for Chinese natives of similar age periods, again emphasizing environment as a factor in influencing blood pressure. Obesity occurred in 10 per cent of the subjects, and in these hypertension was not uncommon. Of the 39 individuals in whom the heart was examined, 6 were found to have hypertensive heart disease and 2 rheumatic valvular disease.

SUMMARY AND CONCLUSIONS

The average blood pressure of Chinese living in Canada for ten years or more is consistently higher (10 mm. Hg) than that reported for Chinese natives. Canadian Chinese have pressures the same as those of the white population. In this series hypertension occurs with surprising frequency (11.2 per cent), in contrast to its rarity in China.

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THE ELECTROCARDIOGRAM OF LOW VOLTAGE

A Report of Fifty Autopsied Cases*

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EVER since electrocardiography came into clinical prominence there has been an effort to correlate the height of excursion of the QRS complex or the voltage of the electrocardiogram with the functional state of the cardiac muscle. Although it has been found that some correlation exists between the extent of the voltage and the function of the heart muscle, it must be remembered that any such parallelism is indirect and subject to certain fortuitous circumstances. This is true because in the human electrocardiogram the height of the QRS complex represents a balance of electrical potential as the conduction wave passes over a complicated, interwoven mass of musculature. Notwithstanding the clinical experience of finding high voltage in patients with markedly decompensated hearts, and low voltage in hearts which are apparently functioning normally, there has been sufficient evidence to warrent looking with caution on the electrocardiogram of low voltage. The low voltage of the electrocardiogram is indicative of one of two things: either the electrical potential associated with the cardiac systole is small, or it has been neutralized by compensatory effects.

Most authorities accept an excursion of 5 mm. or less as low.[1, 2, 3] Pardee, however, sets the lower limit of normal as 7 mm.[4] To fall in this classification of low voltage the excursion of the QRS complex should not exceed these limits in any of the three leads of a properly standardized string. Under such circumstances it is known that low voltage may occur after acute infectious diseases or during circulatory failure of various types. Sprague and White[1] reporting on 57 cases in which the voltage was 5 mm. or less find 77 per cent of the cases related to cardiac failure either resulting from arteriosclerosis or hypothyroidism. Their series also included severe toxic or terminal myocardial states resulting from syphilitic, rheumatic or hypertensive heart disease, mediastino-pericarditis, leucemia, subacute bacterial endocarditis.

As to the prognostic significance of low voltage Hepburn and Jamieson[3] report that 67.6 per cent of their patients died within six months after the first record of low voltage was taken, while 32.4 per cent were living 23.2 months after the first record of low voltage was taken.

In a series of 50 cases of low voltage reviewed by Speckman and Rich[2] there were 14 autopsies. In 10 instances there were enlarged hearts. In

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4 pericardial effusion was found, while 3 had adherent pericardium. Microscopic examination showed abnormalities of the heart muscle in every case of the 14 examined. The most frequent finding was fibrosis of the myocardium. Of this series, 32 of the patients died within six months of the first electrocardiogram of low voltage. As a result of their studies Speckman and Rich conclude that the occurrence of voltage of 5 mm. or less in a patient with heart disease is of serious prognostic importance.

Aside from the above series of autopsied cases there are few reported in the literature. The purpose of the present study is to review 50 cases of low voltage, all of which came to autopsy, and to point out the relationship between the electrocardiogram and the pathological findings. The cases presented all had electrocardiograms in which the maximum excursion did not exceed 7 mm. in a string standardized in the usual manner. All patients appeared on the wards of Cleveland City Hospital and came to autopsy in the hospital. Aside from the above mentioned requisites there was no choice of cases. The autopsy reports from the laboratory of the hospital are based on the diagnoses of several independent workers, so that a fair evaluation of the pathological material is obtained.

Of the 50 cases studied, 41 (82 per cent) were males and 9 (18 per cent) females. The average age was fifty-three years. The oldest patient was seventy-eight years and the youngest eight years. Of these 10 (20 per cent) were negro and 40 (80 per cent) were white.

Advanced cardiac failure was found in 45 of the cases (90 per cent). Cardiac decompensation was present for from two weeks to as long as seventy-two months. The average period of cardiac failure was thirteen months.

On the basis of pathological findings the cases fall into three distinct groups: those which have coronary disease as the primary cardiac lesion; those which possess a cardiac lesion complicated by coronary arteriosclerosis; those which have no involvement of the coronary arteries at all.

The group in which coronary disease is the predominating lesion comprises 21 cases (42 per cent). Table I demonstrates the degree of coronary sclerosis and the associated myocardial and electrocardiographical abnormalities. Coronary arteriosclerosis is present in this group from a moderate degree to complete occlusion with frequent thrombus formation. In several instances myocardial aneurysms are present. This group of coronary arteriosclerotic disease forms the largest single group in the series of low voltage electrocardiograms.

Group II is composed of 17 cases (34 per cent) all of which show a significant degree of coronary sclerosis, but the latter finding cannot be considered the primary lesion. There are 9 instances in this group in which luetic aortic insufficiency is the dominating cardiac abnormality. Although in these, valve leakage and subsequent myocardial fail-

TABLE I

GROUP I. CORONARY DISEASE PRIMARY FACTOR

CASE NO.	AGE	SEX	DEGREE OF CORONARY SCLEROSIS	OTHER PATHOLOGICAL FINDINGS	MAXIMUM VOLTAGE	MECHANISM	OTHER ELECTROCARDIOGRAPHIC FINDINGS
1	60	m	+++	Myomalacia cardis.	6.5 mm.	Fibrillation	Splintering QRS
2	67	m	+++	Myocardial fibrosis. Nephrosclerosis.	2.0 mm.	Normal	Splintering QRS
3	73	m	+++	Myocardial fibrosis. Nephrosclerosis.	6.0 mm.	Fibrillation	T_1 inverted deep Q_3
4	57	m	++++	Myocardial infarct.	4.0 mm.	Fibrillation	T_1–T_2 inverted
5	52	m	++++	2 cardiac aneurysms.	5.0 mm.	Normal	
6	60	m	++++	Coronary thrombosis aneurysm heart.	4.0 mm.	Fibrillation	
7	44	m	++++	Occlusion lt. descending and portion rt.	2.0 mm.	Normal	Splintering
8	58	m	++++	Adhesive pericarditis.	1.0 mm.	Normal	
9	59	m	++++	Occlusion and thrombosis. Adhesive pericarditis.	3.0 mm.	Normal	T_1 inverted
10	47	m	++++	Aneurysm lt. ventricle.	2.0 mm.	Normal	Splintering
11	59	f	++++	Myomalacia cardis.	3.0 mm.	Normal	Splintering
12	56	m	+++	Luetic aortitis.	4.0 mm.	Normal	Arborization block
13	66	m	++++	Aneurysm lt. ventricle.	4.0 mm.	Normal	Splintering and widening QRS
14	69	m	+++	Nephrosclerosis. Marked narrowing coronary orifices.	2.5 mm.	Normal	T_1–T_2 inverted
15	59	m	+++	Cor pulmonale.	5.0 mm.	Normal	Splintering
16	75	m	++++–	Complete occlusion	4.0 mm.	Normal	T_1–T_2 coronary type
17	78	m	++++	Occlusion right. Aneurysm heart.	2.5 mm.	Normal	Splintering QRS
18	56	m	++	Marked hyaline thickening coronary.	3.2 mm.	Normal	
19	62	m	++	Aortic stenosis, arteriosclerotic.	7.0 mm.	Normal	
20	50	m	++	Myomalacia cardis.	4.0 mm.	Normal	Splintering QRS
21	56	m	++	Arterionephrosclerosis.	5.8 mm.	Normal	T_1–T_2 inverted

ure are the most important factors leading to death, nonetheless, the added complication of coronary sclerosis cannot be overlooked. In several instances the coronary orifices are greatly narrowed by a sclerotic process, and this must have interfered with the myocardial blood supply. Similarly there are 3 cases of mitral stenosis in this group, all of which had significant coronary arteriosclerosis. The remainder of the group, 5 cases, show nephrosclerosis, complicated by coronary arteriosclerosis. Table II demonstrates the degree of coronary sclerosis and the associated abnormalities in this group. It is of interest to note that in all cases in which hypertension plays a part, coronary sclerosis is also present.

TABLE II

GROUP II. CORONARY DISEASE COMPLICATING OTHER CARDIAC LESIONS

CASE NO.	AGE	SEX	DEGREE OF CORONARY SCLEROSIS	OTHER PATHOLOGICAL FINDINGS	MAXIMUM VOLTAGE	MECHANISM	OTHER ELECTROCARDIOGRAPHIC FINDINGS
22	63	m	++	Luetic aortitis with ring involvement.	3.0 mm.	Nodal	Splintering
23	73	m	++	Luetic aortic insufficiency.	2.0 mm.	Normal	Splintering
24	54	m	+	Luetic aortic insufficiency.	5.8 mm.	Normal	T_1–T_2 depressed
25	52	m	+	Luetic aortic insufficiency.	5.0 mm.	Normal	T_1–T_2 inverted
26	34	m	++	Luetic aortic insufficiency.	4.0 mm.	Normal	T_1 depressed splintering QRS
27	46	f	+++	Luetic aortic insufficiency.	5.5 mm.	Normal	Arborization block
28	63	m	+++	Luetic aortic insufficiency.	6.0 mm.	Normal	T_2–T_3 inverted splintering
29	44	m	+	Luetic aortic insufficiency.	5.0 mm.	Normal	
30	36	m	++++	Luetic aortic insufficiency.	7.0 mm.	Normal	
31	39	m	+++	Mitral stenosis.	5.0 mm.	Fibrillation	T_2–T_3 inverted
32	26	f	+	Mitral stenosis.	6.5 mm.	Normal	
33	25	m	+	Mitral stenosis.	4.5 mm.	Normal	
34	52	m	+	Nephrosclerosis.	4.0 mm.	Normal	Splintering
35	59	m	+++	Nephrosclerosis.	4.5 mm.	Normal	Splintering
36	71	m	+++	Nephrosclerosis.	3.0 mm.	Fibrillation	Splintering Coronary T
37	60	f	+	Nephrosclerosis.	5.0 mm.	Fibrillation	Splintering
38	56	f	+	Nephrosclerosis.	5.0 mm.	Fibrillation	Splintering

Group III is a miscellaneous group as far as the type of pathological findings is concerned. Acute and chronic infections of various types play the predominating rôle in this group. Of particular interest are the 2 cases of cancer which present no evidence of cardiac disease except such as may accompany cachexia. No doubt the anemia accompanying the malignant disease produced conditions in the cardiac conduction

system or myocardium which caused the low voltage to appear. This miscellaneous group, characterized by an absence of disease of the coronary arteries, comprises 12 cases (24 per cent) of the entire series of 50 cases. Table III illustrates in detail the cases of this type.

TABLE III

GROUP III. MISCELLANEOUS GROUP WITHOUT CORONARY DISEASE

CASE NO.	AGE	SEX	PATHOLOGICAL FINDINGS	MAXIMUM VOLTAGE	MECHANISM	OTHER ELECTROCARDIOGRAPHIC FINDINGS
39	52	m	Mitral and aortic stenosis. Acute and chronic endocarditis.	4.5 mm.	Normal	
40	60	m	Cardiac hypertrophy and dilatation (chronic alcoholism).	5.0 mm.	Fibrillation	
41	31	m	Lobar pneumonia. Acute nephritis.	6.0 mm.		Slurring
42	52	m	Lobar pneumonia.	7.0 mm.	Normal	T_1–T_2 depressed
43	66	m	Tuberculous pericarditis with effusion. Miliary tuberculosis.	7.0 mm.	Normal	T_1–T_2 depressed
44	8	f	Subacute bacterial endocarditis.	3.0 mm.	Fibrillation	Splintering
45	30	f	Chronic and acute endocarditis. Adhesive pericarditis.	4.2 mm.	Normal	T_1–T_2–T_3 isoelectric
46	46	f	Generalized arteriosclerosis. Sclerosis mitral valve. Tuberculous mediastinitis.	5.5 mm.	Normal	Arborization block
47	66	f	Generalized arteriosclerosis.	4.1 mm.	Fibrillation	T_1–T_3 inverted
48	70	m	Brown atrophy of heart. Carcinoma of stomach.	5.5 mm.	Normal	
49	63	m	Carcinoma of stomach with hemorrhage.	4.5 mm.	Fibrillation	
50	59	m	Aortic insufficiency with perivascular infiltration about coronaries. Luetic.	6.0 mm.	Normal	Splintering

The maximum excursion of the QRS complex in any lead of the records studied is 7 mm. The lowest is 1 mm. The average measures 4.54 mm. The most common electrocardiographic abnormality aside from the low voltage is the splintering or slurring of the QRS complex which is found in 26 instances (52 per cent).

T-waves of the cove-plane type, so-called "coronary T-waves," appear in 2 cases (4 per cent). Arborization block is found in 3 instances (6 per cent).

Normal mechanism is present in 37 (74 per cent) of the cases. Nodal rhythm appears once, while fibrillation is present in 12 instances (24 per cent).

In 6 cases (12 per cent) right axis deviation is present. Left axis deviation is found in 20 cases (40 per cent). The remaining 24 cases (48 per cent) show no variation from the normal range.

The accompanying electrocardiograms are typical of the series in this study.

COMMENT

In reviewing the series of 50 cases as a whole, it is apparent that the most frequent pathological finding associated with the electrocardiogram of low voltage is coronary arteriosclerosis. Such sclerosis occurring either as a primary lesion or in association with some other cardiac abnormality, such as luetic or rheumatic heart disease, must interfere with the oxygenation of the conduction system sufficiently to reduce the electrical potential as measured by the electrocardiogram. The presence or absence of sclerosis of the coronary arteries will help to explain why in some instances of luetic aortic insufficiency we find records of high voltage, whereas in others the voltage is low, although in each instance the myocardial incompetency appears to be the same. The same

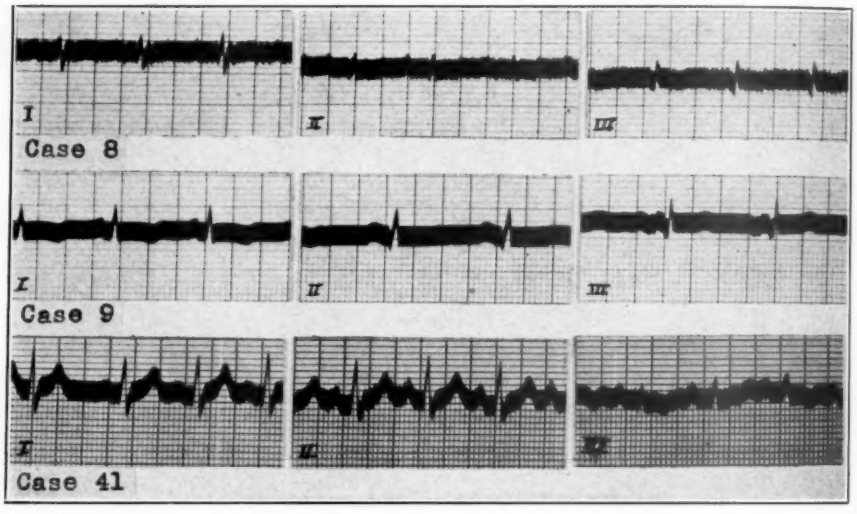

Fig. 1.—Typical electrocardiograms of low voltage.

set of circumstances may explain similar findings in cases of rheumatic heart disease.

In cases of acute or chronic infection or in cachexia (malignant disease) the problem is a different one. In these the toxic substance no doubt affects the conduction system directly and so alters the metabolic processes associated with the spread of the excitation wave through the Purkinje system.

SUMMARY

1. Fifty cases with electrocardiograms of low voltage are reported; all of these came to autopsy.

2. Coronary arteriosclerosis of significant degree was found in 76 per cent of these.

3. In the remaining 24 per cent acute or chronic infections play the most important rôle.

4. The low voltage electrocardiogram is most frequently associated with coronary arteriosclerosis in cases coming to autopsy.

Appreciation is expressed to the Department of Pathology of Cleveland City Hospital for the use of its records.

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AN EARLY CASE OF CORONARY THROMBOSIS NOT HITHERTO REPORTED

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THE development of coronary thrombosis during or following a hearty meal is of common occurrence. Though the pain is usually severe and sometimes referred to the epigastrium, it may be entirely lacking, the victim feeling only extreme weakness accompanied frequently by severe dyspnea.

Because vomiting is common, the condition until recent years was likely to be diagnosed as acute indigestion. Several factors probably contribute to cause an attack at this time. The coronary circulation, due to vessels already diseased, is definitely impaired though symptoms may have been lacking. As the stomach becomes distended, the position of the heart changes somewhat, and as a consequence the already impaired circulation may be further embarrassed. It may be also that the postprandial dilatation of the capillaries of the splanchnic system that accompanies digestion is associated with a diminution of blood flow in the coronary capillaries thus favoring thrombosis. Moreover the leucocytosis and platelet increase that accompany digestion possibly favor clotting.

If the assumption be correct that the patient in the case herein reported suffered from this condition, the case antedates considerably any hitherto reported.

CASE REPORT

G. B., aged eighty years, an itinerant teacher of philosophy, immediately after eating a hearty meal was seized with severe pain and great prostration and died a few hours later. The facts in the case are as follows:

A feast had been provided by the blacksmith of a small village. The menu was diversified and abundant. One dish was especially pleasing to the guest of honor, and he ordered that no one else should be served this particular food. There is some doubt as to just what this was but it seems probable that it consisted of pork. At any rate, after eating all he could, he evidently felt some discomfort, as he ordered that the remaining food be buried in a hole in the ground, remarking that no one else would be able to digest it. Almost immediately thereafter he was taken violently ill and suffered extreme pain. He is said to have passed some blood, probably from the bowels. He tried to conceal his suffering so as not to interfere with the festivity of the occasion and started forth on a journey on foot with some friends but very soon had to stop because of weakness and pain. He sat down on a blanket

and evidently suffered from shock as he complained bitterly of thirst, asking for water three times before it was possible to procure any. Feeling somewhat better, he proceeded on his way, but the increasing pain again forced him to stop, and this time he was evidently too weak to sit, as he lay down. It is stated that he lay on his right side. Inasmuch as one often sees individuals with serious cardiac disease who find that lying on the left side increases their pain, it is perhaps significant that he assumed the right lateral position.

With the great determination that had always characterized his life, he again attempted to proceed but was forced to lie down again; as formerly, he lay on his right side. The pain was obviously much less after he ceased the exertion of walking as he was able to converse with friends at considerable length. As his illness came on at once after dining, quite naturally some one suggested that it was due to something he had eaten. Accordingly, he sent for his host and publicly exonerated him for any responsibility in connection with his illness. This gracious act appears to have been nearer the truth than the generous sufferer may have suspected. He did not succumb until a number of hours after the onset of the attack.

Previous History.—He was the son of a very wealthy man. His mother died soon after his birth. He was evidently much pampered during his early childhood and at eighteen married his cousin. For ten years they lived the usual purposeless life of the idle rich. Becoming very much bored with the futility of this type of existence and being disappointed by his childless marriage, he finally deserted his wife and the baby which arrived too late to conquer his ennui. For six years he lived in the open, subsisting on a very poorly balanced and inadequate diet especially low in protein. It consisted chiefly of dry mosses, roots and wild fruits. As the result of this diet he became exceedingly emaciated. Later his manner of living and diet changed materially, but he was always temperate in his habits. In the main, his health appears to have been good.

Because of his catholic ideas, he often dined with individuals of widely different social stations. Thus we see him as the guest of honor at a feast given by certain wealthy nobles and shortly thereafter he was entertained at an even more elaborate affair, the hostess being a well-known courtesan. Not long after the latter dinner party he became very ill. The nature of this sickness is unknown, but it seems probable that it was some sort of an infection as he became much emaciated and his death was reported. He appears to have recovered by the time of the party given by the blacksmith but it may be that this infection predisposed him to coronary thrombosis as sometimes appears to be the case.

It is of interest further that he was of the square-shouldered or pyknic type, as such individuals are thought to be especially prone to occlusion of the coronary vessels.

The old gentleman whose final illness we have been considering died in the fifth century B.C. His name was Gotama Buddha.

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PARADOXICAL EMBOLISM OF THE CORONARY ARTERY*

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WHILE acute occlusion of the coronary arteries occasioned by endarterial changes and thrombosis or by spasm is a common clinical diagnosis, made daily and confirmed frequently at the section table, gross embolism of these vessels is apparently a very rare condition, receiving scant attention in works on cardiology or special pathology[1, 2, 3, 4] and but little more in the periodicals.[5, 6]

A recent comprehensive review of the literature by Saphir[7] disclosed but eleven cases of true coronary embolism. These were associated with intrinsic cardiac or vascular disease. Still rarer are cases of paradoxical embolism of these vessels; the literature contains only the cases of Wolff and White,[8] of Thompson and Evans[9] (a case of tumor embolus) and the first of Saphir, and these were also associated with intrinsic cardiac or vascular pathology. Because of the rarity of the lesion, the sudden and unusual clinical course, and the complete absence of associated cardiac disease, the following case is being reported.

CASE REPORT

Mrs. M. R., aged forty-seven years, white, entered the medical service of Staten Island Hospital with the chief complaint of upper abdominal cramps of three days' duration.

Her family history and marital history were unimportant. She had had typhoid fever at twelve years, pneumonia at nineteen years, a two-stage thyroidectomy at thirty-four years, and a panhysterectomy at forty-four years.

Her present illness dates back to six days prior to entry when she developed vague aches and pains and was treated by her family physician for "grippe." A few days later she developed vomiting, diarrhea, and abdominal cramps. Except for slight dyspnea on exertion during the past three years, and an occasional attack of "dull ache" over the precordium, transient and related to excitement, the rest of the history was unimportant.

Physical examination on admission revealed a fairly well-developed but undernourished, white, middle-aged female, with an anxious expression and an appearance of exhaustion. Emotionally she was unstable. Temperature 98.6°, pulse 90 and respirations 20. Urine showed a slight trace of albumin and the blood showed a secondary anemia and a relative lymphocytosis.

Head, scalp, ears, nose, throat and lungs gave negative signs. On ophthalmoscopic examination there was recent hemorrhagic exudate on the temporal side of the right disc. There were two well-healed scars over the anterior aspect of the neck.

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Examination of the heart was not particularly remarkable. Apex beat was not seen or felt. No thrills. No enlargement. Sounds were regular and of good quality. Ventricular rate equalled pulse rate (100). Blood pressure was 100/75 mm.

The admission diagnosis was gastroenteritis, and she was given a low residue diet, bismuth salts and sedatives. Within a few days there was a decided improvement. It is perhaps worthy of mention here that she had no symptoms referable to the cardiorespiratory system during the course of her stay in the hospital.

On the sixth day of her stay in the hospital, while lying flat on her back she was suddenly seized with a sharp, agonizing substernal pain. Within fifteen minutes she was pronounced dead.

Autopsy performed two hours after death disclosed a well-developed and fairly well-nourished middle-aged white female showing healed thyroidectomy and trans-

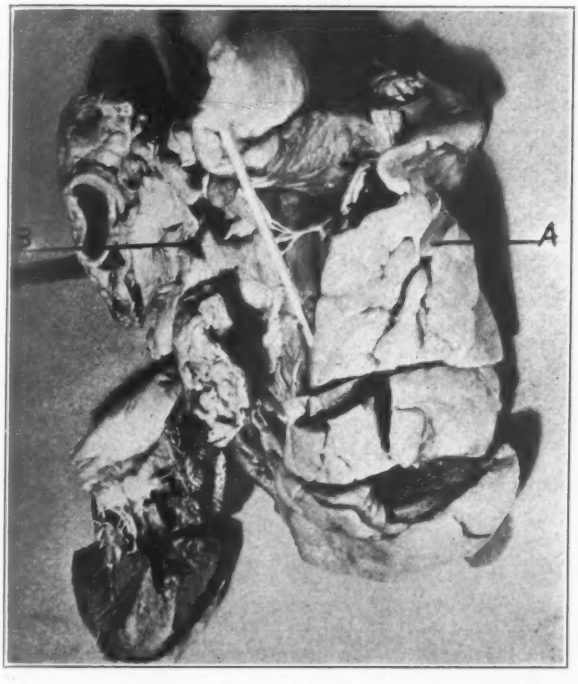

Fig. 1.—Heart opened and showing the embolus in left coronary artery (A), and the patent foramen ovale, with probe inserted (B).

verse lower abdominal operative scars. The face, oral mucosae, finger and toe nails were markedly cyanotic, the remainder of the skin was somewhat less cyanotic. There was no rigor or post-mortem discoloration in any portion of the body; the entire body was quite warm. There was a slight but definite pitting edema of the entire left lower extremity, most marked over the ankle but present also over the buttock. There was no edema in any other portion, and there were no evidences of varicose veins in either extremity.

On opening the thoracic cavity, several complete auricular contractions were observed, tapering off into fibrillary twitches of the left ventricle, while the lungs rapidly deepened in red color and the abdominal veins and pulmonary artery became visibly distended with venous blood. The heart itself weighed 300 gm.; the endocardium, pericardium and valves were all smooth, glistening and translucent throughout; the myocardium was of good tone; all somewhat paler than usual. The foramen

ovale presented an opening 0.5 cm. in diameter. In the anterior descending branch of the left coronary artery was a soft, lamellated gray red thrombus, 1 cm. in length and 0.3 cm. in diameter, which completely plugged the vessel from a point just beyond its origin distalward for about 0.6 cm., the embolus being curled on itself; there was no propagated or retrograde thrombus. The plug was very easily removed from the vessel, disclosing the underlying intima smooth, glistening, and utterly devoid of atheromatous change. A similarly smooth and glistening intima was present in the other coronary branches. The aorta presented a few pinhead sized soft yellowish atheromatous patches in the intima of the arch, everywhere, however, covered by smooth and glistening surfaces. In fact the entire aorta and its branches were surprisingly free of atherosclerotic changes. No aortic valvular, commissural, or coronary orificial changes suggestive of syphilis were present. No thrombi were present in either auricular appendage. There were no vascular anomalies except for the patent foramen ovale.

The lungs were well aerated, not edematous, but congested. Their entire vascular tree, arterial and venous, showed no intrinsic or thrombotic changes. The abdominal viscera were moderately congested. In the left kidney a recent white infarct a few millimeters in diameter was present on the midanterior surface. The uterus, left tube and ovary and right tube were absent; the right ovary was firm and contained several corpora lutea of varying size and a few retention cysts. The entire vaginal vault was covered by old peritoneal adhesions.

The left femoral vein was thickened. Just distal to its entrance into the iliac vein, it was partially occluded by firm brownish red tissue, to the proximal end of which a grayish red, softer thrombus, similar grossly to that found in the coronary artery, was still attached. The intima under both types of thrombus was dulled and roughened when the latter was detached. The remaining pelvic and abdominal veins, and the right femoral, thoracic, and cervical veins were unchanged.

Sections of the embolus in the coronary artery and similar fragments in the femoral vein were composed of lamellated platelet-erythrocyte thrombus with some admixture of polymorphonuclear leucocytes. Sections of the firmer brown red femoral thrombus consisted of partially canalized hyalinized fibrous tissue which merged, without demarcation, with the venous wall. The latter showed elastica fragments in the contact zone but no definite elastica. The media was fibrosed but not cell-infiltrated; the adventitia was unaltered.

Sections of the kidney through the infarcted area disclosed the usual picture of a bland infarct. The remainder of the kidneys, as well as the lungs and abdominal viscera, presented the picture of an acute passive congestion.

Sections of the heart through interventricular septum and adjoining portions of the ventricles showed the cytoplasm and nuclei swollen and poorly stained. Elsewhere there were no cellular changes and no evidence of recent or old rheumatic, syphilitic, or arteriosclerotic vascular changes.

DISCUSSION

The possibility of embolism in this case was entirely overlooked clinically because of the apparent absence of a source. The precordial pain and the dyspnea, not typically anginoid in character, might have suggested cardiovascular occlusive changes, particularly in the absence of any evidences of hypertension or organic vascular disease. Had the buttock and ankle edema of the left lower extremity present at the autopsy table been noted ante-mortem, it might have given a suggestive lead to a potential source of embolism.

Of interest was the continued cardiac contraction after clinical death and at the autopsy and the visible termination in ventricular fibrillation, both findings not of frequent record. The case is of further interest in that it is the only one on record in which a long antecedent and already organized venous thrombosis has given rise to coronary embolism. In other respects, such as the branch involved and the mode of death, it corresponds to the general findings in Saphir's review. No such factors as depletion of the pulmonary circulation, or significant differences in the caliber between the aortic and coronary orifices were present in this case to explain the coronary involvement, as suggested in Saphir's review. In view of the embolic phenomena in other organs, we feel that the coronary involvement was purely incidental to a general embolizing process.

SUMMARY

A case of acute coronary occlusion due to an embolus from an old thrombosis of the femoral vein in the presence of a patent foramen ovale is reported. There were no associated arterial or endocardial changes. The factors in its production are discussed briefly.

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Leroy Crummer

APRIL 15, 1872—JANUARY 2, 1934

THE recent lamented death of Doctor Crummer removes a nationally known and greatly respected figure in the fields of internal medicine and medical history.

After being graduated from the Northwestern University Medical School in 1896, Doctor Crummer lived most of his professional life in Omaha, where ultimately he became professor of medicine in the University of Nebraska College of Medicine (1919-1925).

During the War his services were requisitioned by the Army, and he rendered notable service as a teacher of physical diagnosis in the school for civilian medical officers established at Camp Greenleaf, Tenn.

His professional interests were especially keen in the field of heart diseases, and the popularity of his modest volume, *Clinical Features of Heart Disease,* attests his soundness as a clinician and teacher.

During the last few years of his life, an invalid himself from heart disease, Doctor Crummer resided in Los Angeles and devoted himself almost entirely to his fine library and to studies in medical history. His distinction in this field was recognized at both the University of California and the University of Southern California by his appointment to a professorship in medical history.

As an honored member of the Advisory Editorial Board of the AMERICAN HEART JOURNAL his loss is deeply felt.

Department of Reviews and Abstracts

Book Review

VERHANDLUNGEN DER DEUTSCHEN GESELLSCHAFT FÜR KREISLAUFFORSCHUNG VI TAGUNG. Edited by Dr. Bruno Kisch. Theodor Steinkopff, Dresden and Leipzig, 1933, 276 pages.

The sixth annual meeting of the Deutsche Gesellschaft für Kreislaufforschung was given over to a discussion of the relation between the circulatory and nervous systems. The first part of the program is experimental, the second clinical in viewpoint; both parts contain interesting and instructive papers.

E. H.

STROPHANTHIN-THERAPIE. By Professor Dr. A. Fraenkel, Heidelberg, with the collaboration of Dr. R. Thauer, Frankfort, Berlin, Julius Springer, 1933, 148 pp.

The introduction affords an accurate guide to what one may anticipate in the author's treatment of the subject, in that he declares his preference for the treatment of cardiac insufficiency by means of the intravenous injection of strophanthin. The table of contents permits one to turn at once to any particular phase of this subject—history, botany, pharmacognosy, chemistry, pharmacology, or therapy—in which one may be especially interested. Each division is followed by references to the literature arranged alphabetically. The several bibliographies include references to more than 750 papers. The monograph itself being mainly a review of the essential literature, the present reviewer finds it difficult to give anything approaching a satisfactory review of it without exceeding the space permitted.

Some thirty-five pages are devoted to the division entitled, "The Pharmacology of Strophanthin." This division in reality is devoted mainly to the pharmacology of digitalis, but, as the author states, the actions of digitalis and strophanthin are qualitatively similar after they have entered the blood stream. The author has shown discernment in the selection of papers which he has reviewed, but, naturally, no monograph of this size can fail to omit reference to some papers that may be considered important. The author refers repeatedly to the work of Weese, who compared the amounts of digitoxin and strophanthin taken up by the heart with those fixed in other organs, and since he bases important conclusions on this work, it may be proper to state that reference to Weese's paper shows that his results do not uniformly substantiate his conclusions. The discussion of the toxic side actions of the digitalis bodies is confined almost exclusively to that of nausea and vomiting. The biological standardization of the digitalis bodies is discussed concisely, but the author considers it of value only as showing the degree of constancy of activity of a given preparation. That view is tenable for one who administers digitalis bodies orally, much more than in the case of one who injects them intravenously; in the latter case the actual activity of different substances is more nearly proportional to the indicated activity than when they are administered orally. More than half of the monograph (about eighty pages) is devoted to the clinical use of the digitalis bodies, with arguments in favor of the intravenous use of strophanthin. This is

presented systematically and includes the history of intravenous therapy, the technic, the observation of the use of strophanthin in practice, indications and dosage, with numerous case histories, tracings, electrocardiograms and x-ray photographs of the heart.

The author is obviously impressed with the superiority of strophanthin over other substances designed for intravenous injection, but when he states that one of the advantages of strophanthin is its relative nontoxicity (''relativen Ungiftigkeit''), one wonders just what is meant, because it is very well known that the fatal dose of a digitalis body closely parallels its therapeutic activity. If by ''Ungiftigkeit'' the author means its relatively slight nauseant and emetic action, it is at least understandable, because strophanthin is relatively less nauseant than some of the proprietary preparations with which the author compares it; but this statement must not be understood as indicating that it is less dangerously toxic. In pointing out the advantages of strophanthin over nearly similar substances, the argument is occasionally strained (page 77).

When one has read the monograph carefully, one is impressed with the difficulties of treating cardiac disease wisely without that mastery of the subject which can be acquired only by long, patient, painstaking observations of symptoms and of the varying effects of the therapeutic use of digitalis. In this country, at least, it is the nearly unanimous opinion of cardiologists that the oral administration of digitalis suffices for the treatment of nearly all patients with cardiac disease who are capable of responding to it with any form of administration, and it must be apparent to all that the intravenous injection of strophanthin is dangerous in the hands of any but the well-informed cardiologist, though it is beyond question that nearly every physician will occasionally see a patient suffering with acute cardiac failure who needs an intramuscular or intravenous injection of one of the digitalis bodies.

A word of praise is due the publisher. This monograph is beautifully printed and the illustrations and tracings show exquisite workmanship, so that it is a pleasure to read it.

R. A. H.